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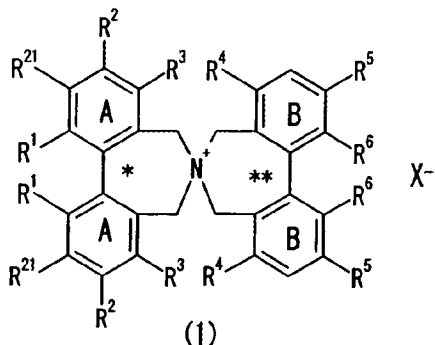
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(54) **OPTICALLY ACTIVE AMMONIUM SALT COMPOUND, PRODUCTION INTERMEDIATE THEREOF AND METHOD FOR PRODUCING SAME**

(57) An optically active quaternary ammonium salt compound represented by formula (1),



wherein R¹ represents a halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl

which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted; R² and R²¹ each independently represents hydrogen, halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted; one of combinations of R¹ and R²¹, and R² and R²¹, may bond to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylene monooxy which is optionally substituted, or a C₁₋₆ alkylene dioxy which is optionally substituted; R³ and R⁴ each independently represents hydrogen, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, with a proviso that R³ and R⁴ are not hydrogen at the same time; R⁵ represents hy-

drogen, halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, or a C₂₋₈ alkynyl which is optionally substituted;

R⁶ represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is

linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, or a C₂₋₈ alkynyl which is optionally substituted, and R⁵ and R⁶ may bond to form an aromatic ring which is optionally substituted;

ring A and ring B do not have a same substituent at the same time;

symbols * and ** represent an optical activity having an axial chirality; and

X⁻ represents an anion.

Description

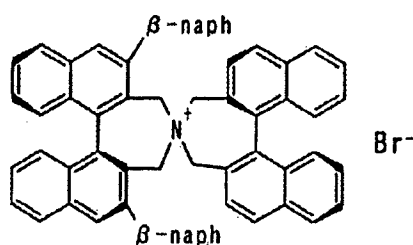
[Technical Field]

[0001] The present invention relates to a compound of an optically active quaternary ammonium salt which is useful as a chiral phase transfer catalyst and more specifically, relates to a novel optically active quaternary ammonium salt, and an intermediate and production method for producing said compound.

Priority is claimed on Japanese Patent Applications No. 2005-059694, filed March 3, 2005, and No. 2005-192757, filed June 30, 2005, the contents of which are incorporated herein by reference.

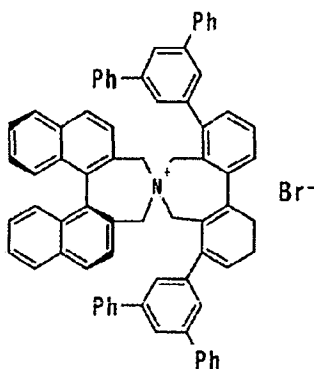
[Background Art]

[0002] Many compounds regarding optically active spiro quaternary ammonium salts have been known to date. Examples thereof include the compound described in Patent document 1 and represented by the following formula

[0003]

[0004] and the compound described in Patent document 3, and the documents disclose that these compounds perform extremely effectively as a phase transfer catalyst for synthesizing optically active α -amino acids regardless of being natural or not. However, the optically active spiro quaternary ammonium salts described in these documents are expensive since they are constituted from two kinds of binaphthyl derivatives having different substituents, and thus they are not necessarily satisfactory for industrial use.

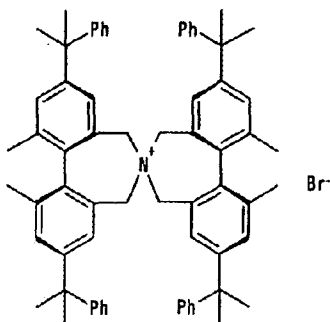
[0005] Moreover, the compound represented by the following formula is described in Patent document 2.

[0006]

However, because the compound is optically active only on one side, the reaction time is long, and thus the compound is not necessarily satisfactory for industrial use.

[0007] Furthermore, the compound represented by the following formula is described in Patent document 4. However, since the spiro quaternary ammonium salts described in these documents are constituted of two kinds of optically active biphenyl derivatives which have the same substituents, there are limits in catalyst design, and thus the salts are not necessarily satisfactory for industrial use.

[0008]



[0009] For this reason, the development of an optically active spiro quaternary ammonium salt which is effective as a phase transfer catalyst for synthesizing optically active α -amino acids and which is readily produced and is also practical, has been desired.

[0010]

- [Patent document 1] Japanese Laid-Open Patent Application No. 2001-48866
- [Patent document 2] Japanese Laid-Open Patent Application No. 2002-326992
- [Patent document 3] Japanese Laid-Open Patent Application No. 2003-81976
- [Patent document 4] Japanese Laid-Open Patent Application No. 2004-359578

[Disclosure of the Invention]

[Problems to be Solved by the Invention]

[0011] The present invention is made to solve the aforementioned problems of the prior art regarding the compounds of optically active quaternary ammonium salts which are useful as chiral phase transfer catalysts. The object of the present invention is to provide a compound having excellent effects in synthesizing optically active amino acids regardless of being natural or not, and a production method capable of producing said compound to industrial advantage.

[Means for Solving the Problem]

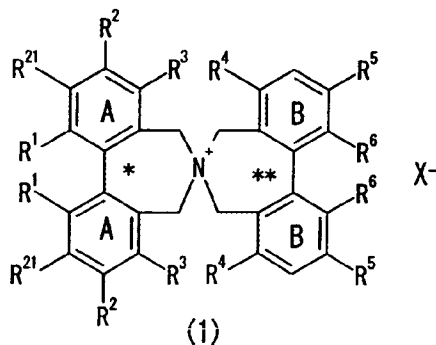
[0012] The present inventors studied intensively in order to solve the above problems and discovered the following to complete the present invention. That is, optically active spiro quaternary ammonium salts, which are constituted from two kinds of biphenyl derivatives having different substituents or from a biphenyl derivative and binaphthyl derivative, and which can be used as a catalyst having excellent effects in synthesizing optically active amino acids and which are industrially useful, as well as a method for readily producing said quaternary ammonium salts.

[0013] In the present invention, the discovered method for readily producing the spiro quaternary ammonium salts is based on kinetic resolution. According to said production method, for example, even when a biphenyl derivative, which is a material compound, has no optical activity, a compound of an optically active quaternary ammonium salt having two axial asymmetries can readily be obtained by reacting with an optically active azepine derivative. During this process, it is also possible to recover the biphenyl derivative which is not involved in the reaction as an optically active substance. In addition, when a biphenyl derivative, which is a material compound, has an optical activity, likewise, a compound of an optically active quaternary ammonium salt having two axial asymmetries can readily be obtained by reacting with an azepine derivative which has no optical activity, and it is also possible to recover the azepine derivative, which is not involved in the reaction, as an optically active substance.

[0014] Furthermore, another basis constituting the method for readily producing the spiro quaternary ammonium salts which have been discovered in the present invention is the simple production method of azepines which are important production intermediates for producing the spiro quaternary ammonium salts. According to the present production method, by reacting a 2,2'-bis(substituted methyl)biaryl compound, which has a substituent at the 3,3'-positions, with ammonia, corresponding azepines can readily be obtained.

[0015] That is, a first aspect of the present invention relates to an optically active quaternary ammonium salt compound represented by the formula (1)

[0016]



[0017] (in the formula, R¹ represents a halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;

R² and R²¹ each independently represents hydrogen, halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted and one of combinations of R¹ and R²¹, and R² and R²¹, may bind to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylenedioxy which is optionally substituted, or a C₁₋₆ alkylenedioxy which is optionally substituted;

R³ and R⁴ each independently represents hydrogen, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, with a proviso that R³ and R⁴ are not hydrogen at the same time;

R⁵ represents hydrogen, halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, or a C₂₋₈ alkynyl which is optionally substituted;

R⁶ represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, or a C₂₋₈ alkynyl which is optionally substituted, and R⁵ and R⁶ may bond to form an aromatic ring which is optionally substituted;

ring A and ring B do not have a same substituent at the same time;

symbols * and ** represent an optical activity having an axial chirality; and X⁻ represents an anion).

[0018] As the quaternary ammonium salt compound represented by the formula (1) the following compounds are preferable:

a compound in which R² is hydrogen and R²¹ is halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;

a compound in which R¹, R², and R²¹ each independently represents a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic;

a compound in which R¹ is a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, and R² and R²¹ bond to form a C₁₋₆ alkylenedioxy which is optionally substituted;

a compound in which R¹ and R²¹ each independently represents a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, and R² is hydrogen;

a compound in which R¹ and R²¹ bond to form a C₁₋₆ alkylenedioxy which is optionally substituted, and R² is hydrogen, fluorine, chlorine, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;

a compound in which R¹ is fluorine, chlorine, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, or a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, and R² and R²¹ bond to form a C₁₋₆ alkylenedioxy which is optionally substituted;

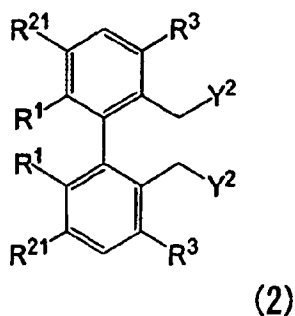
a compound in which R³ represents a C₆₋₁₄ aryl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl), a C₃₋₈ heteroaryl (which

is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl), or a C₇₋₁₆ aralkyl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl); and R⁴ is hydrogen;
 5 a compound in which R³ represents hydrogen and R⁴ is a C₆₋₁₄ aryl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl), a C₃₋₈ heteroaryl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl), or a C₇₋₁₆ aralkyl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl); and
 10 a compound in which X⁻ is an anion of halogen, OH⁻, BF₄⁻, PF₆⁻, HSO₄⁻, an anion of C₁₋₆ dialkylsulfate which is optionally substituted and which is linear, branched, or cyclic, an anion of C₁₋₆ alkylsulfonate which is optionally substituted and which is linear, branched, or cyclic, an anion of C₆₋₁₄ arylsulfonate which is optionally substituted, or an anion of C₇₋₁₆ aralkylsulfonate which is optionally substituted.

[0019] In addition, a second aspect of the present invention relates to:

(i) an optically active bisbenzyl compound or a racemic bisbenzyl compound represented by the formula (2)

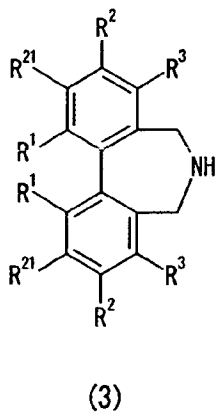
[0020]



[0021] (in the formula, R¹, R²¹, and R³ are the same as above and Y² represents a leaving group) which has axial chirality; and

(ii) a racemic azepine derivative or an optically active azepine derivative represented by the formula (3)

[0022]



[0023] (in the formula, R¹, R², R²¹, and R³ are the same as above).

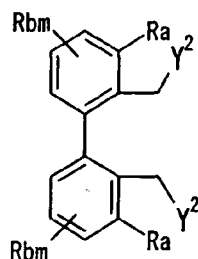
[0024] A third aspect of the present invention is a production method of an azepine derivative characterized in that a biphenyl derivative represented by the formula (4)

[0025]

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(4)

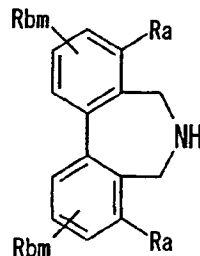
[0026] (in the formula, Ra represents a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted; Rb represents halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted, and Rb may bond with each other to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylenemonooxy which is optionally substituted, a C₁₋₆ alkylenedioxy which is optionally substituted, or an aromatic ring which is optionally substituted; and m is 0 or represents an integer of 1 to 3 and Rb may be different substituents to each other when m is 2 or more); and ammonia are reacted to produce the azepine derivative represented by the following formula (5)

[0027]

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(5)

[0028] (in the formula, Ra, Rb, and m are the same as above). This azepine derivative is useful as a production intermediate of the compound represented by the formula (1).

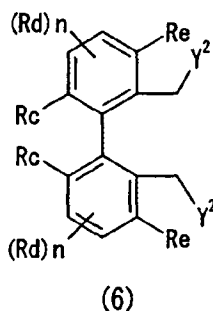
[0029] A fourth aspect of the present invention is a production method of an optically active quaternary ammonium salt compound characterized in that,

(i) an optically active bisbenzyl derivative represented by the formula (6)

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[0030]

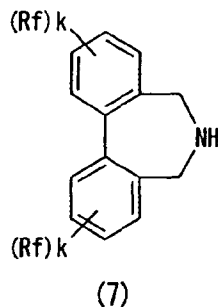
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[0031] (in the formula, Rc represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted; Rd and Re each independently represents halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, and Rd may bond with each other to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylidenemonooxy which is optionally substituted, or a C₁₋₆ alkylidenedioxy which is optionally substituted, and n is 0 or represents an integer of 1 to 2 and Rd may be different substituents to each other when n is 2; and Y² is the same as above);

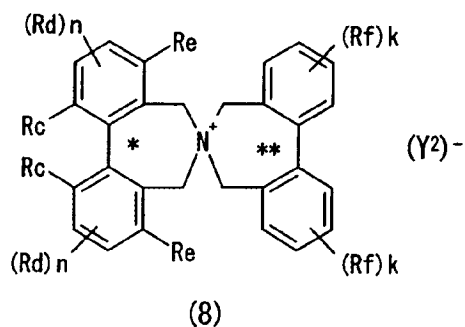
and racemic azepine derivative represented by the formula (7)

[0032]



[0033] (in the formula, Rf represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, and k is 0 or represents an integer of 1 to 4 and Rf may be different substituents to each other when k is 2 or more and Rf may bond with each other to form an aromatic ring which is optionally substituted); are reacted to produce the optically active quaternary ammonium salt compound represented by the formula (8)

[0034]

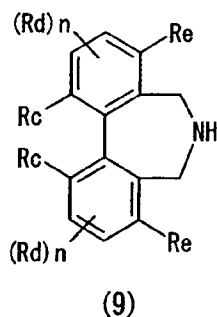


[0035] (in the formula, Rc, Rd, Re, Rf, n, k, and symbols * and ** are the same as above); and

(ii) the production method of an optically active quaternary ammonium salt compound represented by the formula (8) characterized in that the racemic bisbenzyl derivative represented by the formula (6) and optically active azepine derivative represented by the formula (7) are reacted.

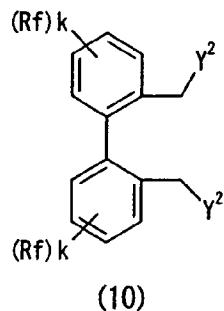
[0036] A fifth aspect of the present invention is a production method of an optically active quaternary ammonium salt compound characterized in that an optically active azepine derivative represented by the formula (9)

[0037]



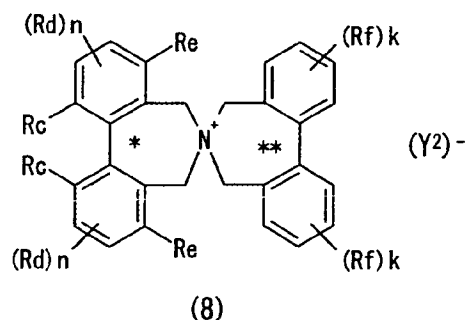
[0038] (in the formula, Rc, Rd, and n are the same as above); and racemic bisbenzyl derivative represented by the following formula (10)

[0039]



[0040] (Rf, k, and Y² are the same as above); are reacted to produce the optically active quaternary ammonium salt compound represented by the following formula (8)

[0041]



[0042] (in the formula, Rc, Rd, Re, Rf, n, k, and symbols * and ** are the same as above); and

(ii) a production method of the optically active quaternary ammonium salt compound represented by the formula (8) characterized in that the racemic bisbenzyl derivative represented by the formula (9) and optically active azepine derivative represented by the formula (10) are reacted.

[Effects of the Invention]

[0043] The optically active quaternary ammonium salt compound of the present invention can be produced in an industrially advantageous method and has an excellent catalytic effect on the synthesis of optically active amino acids. In addition, according to the production method of the present invention, the compounds of optically active quaternary ammonium salts can be industrially advantageously produced due to kinetic resolution.

[Best Modes for Carrying Out the Invention]

[0044] The present invention will be described in detail below.

Examples of halogens in the present specification include each atom of fluorine, chlorine, bromine, and iodine.

[0045] Examples of the C₁₋₈ alkyl, which is linear, branched, or cyclic, of the C₁₋₈ alkyl which is linear, branched, or cyclic, and which is optionally substituted, include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, neopentyl, hexyl, isohexyl, heptyl, isoheptyl, octyl, isooctyl, cyclopropyl, cyclobutyl, 2-methylcyclopropyl, cyclopropylmethyl, cyclopentyl, and cyclohexyl.

[0046] Examples of the C₂₋₈ alkenyl of the C₂₋₈ alkenyl, which is optionally substituted, include vinyl, 1-propenyl, 2-propenyl, isopropenyl, 1-butenyl, 2-butenyl, 3-butenyl, 1-pentenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 1-methyl-2-butenyl, 1-methyl-3-butenyl, 1,1-dimethyl-2-propenyl, 3-methyl-2-butenyl, 1-hexenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-methyl-1-pentenyl, 3-methyl-1-pentenyl, 4-methyl-1-pentenyl, 2-methyl-2-pentenyl, 3-methyl-2-pentenyl, 2-ethyl-1-butenyl, 3,3-dimethyl-1-butenyl, 1-heptenyl, 2-heptenyl, 3-heptenyl, 1-octenyl, 2-octenyl, 3-octenyl, and 4-octenyl.

[0047] Examples of the C₂₋₈ alkynyl of the C₂₋₈ alkynyl, which is optionally substituted, include ethynyl, 1-propynyl, 2-propynyl, 1-butylnyl, 2-butylnyl, 3-butylnyl, 1-pentylnyl, 2-pentylnyl, 3-pentylnyl, 4-pentylnyl, 4-methyl-1-pentylnyl, 1-hexynyl, and 1-octynyl.

[0048] Examples of the C₆₋₁₄ aryl of the C₆₋₁₄ aryl, which is optionally substituted, include phenyl, 1-naphthyl, 2-naphthyl, 1-anthryl, 2-anthryl, 9-anthryl, 1-phenanthryl, 2-phenanthryl, 3-phenanthryl, 4-phenanthryl, 9-phenanthryl, and 10-phenanthryl.

[0049] The C₃₋₈ heteroaryl of the C₃₋₈ heteroaryl, which is optionally substituted, is monocyclic, polycyclic, or a condensed ring which contains 1 to 4 atoms of N, O, and S and these atoms may be the same or different. Specific examples of the C₃₋₈ heteroaryl include 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-quinonyl, 3-quinonyl, 4-quinonyl, 5-quinonyl, 6-quinonyl, 7-quinonyl, 8-quinonyl, 2-indolyl, 3-indolyl, 4-indolyl, 5-indolyl, 6-indolyl, 7-indolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyrrolidyl, 3-pyrrolidyl, 2-imidazolyl, 4-imidazolyl, 5-imidazolyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, 2-thiazolyl, 4-thiazolyl, and 5-thiazolyl.

[0050] The alkyl moiety of the C₁₋₈ alkoxy, which is linear, branched, or cyclic, of the C₁₋₈ alkoxy which is linear, branched, or cyclic, and which is optionally substituted, is the same as the aforementioned alkyl. Specific examples of the C₁₋₈ alkoxy include methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, sec-butoxy, tert-butoxy, pentyloxy, isopentyloxy, hexyloxy, heptyloxy, octyloxy, cyclopropoxy, cyclobutoxy, 2-methylcyclopropoxy, cyclopropylmethoxy, cy-

clopentyloxy, and cyclohexyloxy.

[0051] Examples of the C_{7-16} aralkyl of the C_{7-16} aralkyl, which is optionally substituted, include benzyl, 1-phenylethyl, 2-phenylethyl, 1-methyl-1-phenylethyl, 1-naphthylmethyl, and 2-naphthylmethyl.

[0052] Examples of X^- include anions such as anions of halogens like fluorine, chlorine, bromine, and iodine; OH^- ; BF_4^- ; PF_6^- ; SCN^- ; HSO_4^- ; anions of C_{1-6} dialkyl sulfate which is optionally substituted and which is linear, branched, or cyclic; anions of C_{1-6} alkyl sulfonate which is optionally substituted and which is linear, branched, or cyclic; anions of C_{6-14} aryl sulfonate which is optionally substituted; and anions of C_{7-16} aralkyl sulfonate which is optionally substituted.

[0053] The alkyl moieties of C_{1-6} dialkyl sulfate which is optionally substituted and which is linear, branched, or cyclic and of C_{1-6} alkyl sulfonate which is optionally substituted and which is linear, branched, or cyclic are the same as the aforementioned alkyl. Specific examples of the C_{1-6} dialkyl sulfate and C_{1-6} alkyl sulfonate include dimethyl sulfate, methyl sulfonate, ethyl sulfonate, propyl sulfonate, and butyl sulfonate.

[0054] The aryl moiety of C_{6-14} aryl sulfonate group which is optionally substituted is the same as the aforementioned aryl. Specific examples of the C_{6-14} aryl sulfonate include phenylsulfonate, p-toluenesulfonate, and naphthylsulfonate.

[0055] The aralkyl moiety of C_{7-16} aralkyl sulfonate group which is optionally substituted is the same as the aforementioned aralkyl. Specific examples of the C_{7-16} aralkyl sulfonate include benzylsulfonate and phenethylsulfonate.

[0056] Examples of the aromatic ring which is formed by the bonding of R^5 and R^6 and which is optionally substituted include a benzene ring and naphthalene ring.

[0057] The C_{1-6} alkylene of the C_{1-6} alkylene, which is optionally substituted, is represented by the formula $-(CH_2)_n-$ (in the formula, n represents an integer of 1 to 6). Specific examples of the compounds, in which R^1 and R^{21} or R^2 and R^{21} are bonded, include the compounds having the following structures.

[0058]

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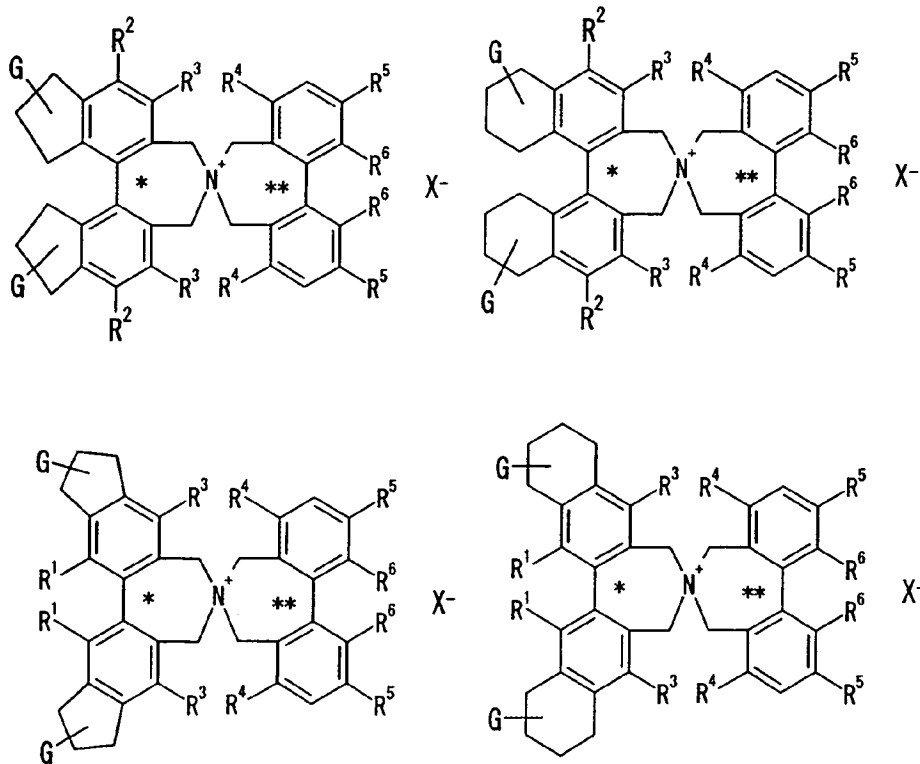
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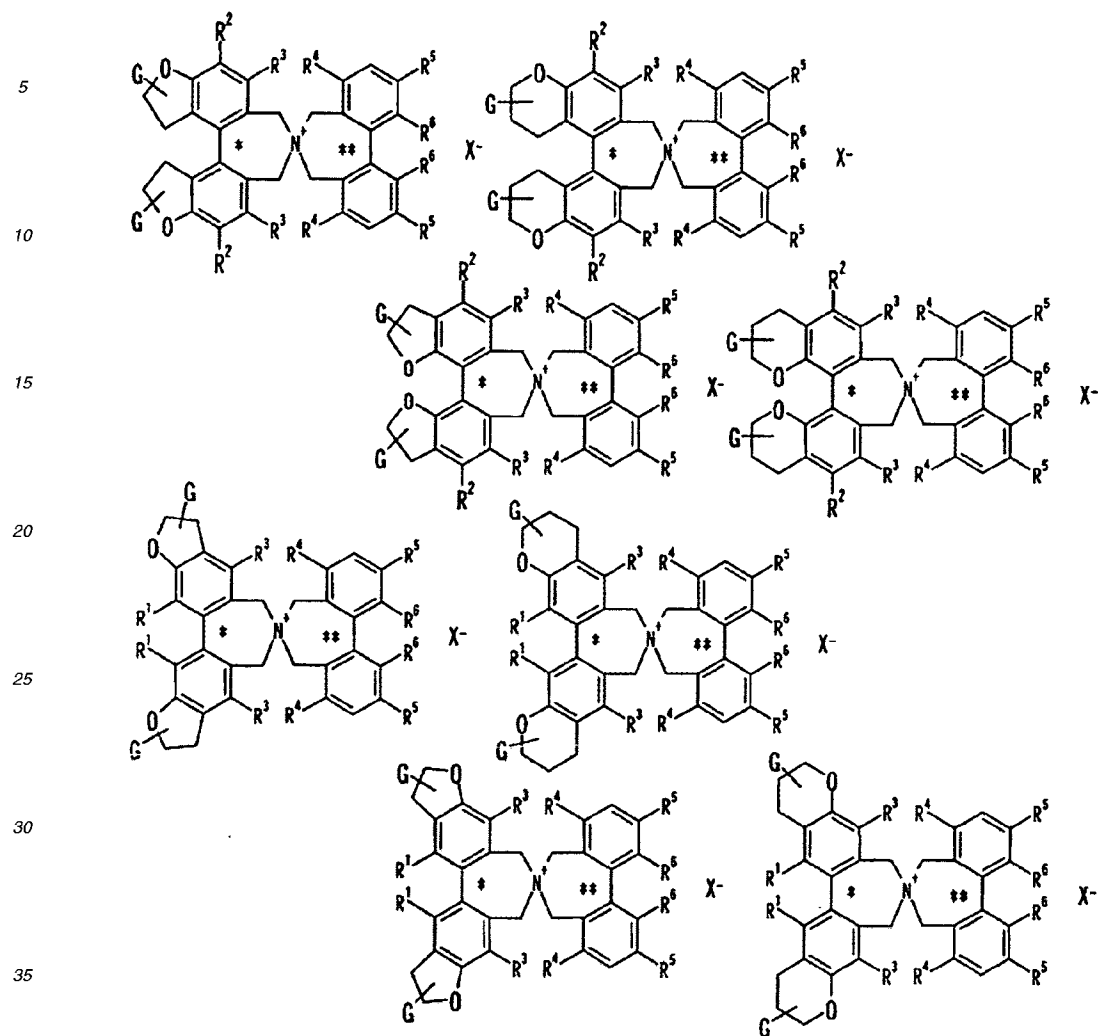
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(In the formula, G represents a substituent.)

[0059] The C_{1-6} alkylenemonooxy of the C_{1-6} alkylenemonooxy, which is optionally substituted, is represented by the formula $-O(CH_2)_n-$ or $-(CH_2)_nO-$ (in the formula, n represents an integer of 1 to 6). Specific examples of the compounds, in which R^1 and R^{21} or R^2 and R^{21} are bonded, include the compounds having the following structures.

[0060]



(In the formula, G represents a substituent.)

[0061] The C_{1-6} alkylendioxy of the C_{1-6} alkylendioxy, which is optionally substituted, is represented by the formula $-O(CH_2)_nO-$ (in the formula, n represents an integer of 1 to 6). Specific examples of the compounds, in which R^1 and R^{21} or R^2 and R^{21} are bonded, include the compounds having the following structures.

[0062]



20

The alkyl moiety, aryl moiety, and aralkyl moiety in the C₁₋₈ alkylsulfonyloxy which is optionally substituted and which is linear, branched, or cyclic, C₆₋₁₄ arylsulfonyloxy which is optionally substituted, and C₇₋₁₆ aralkylsulfonyloxy which is optionally substituted, are the same alkyl, aryl, and aralkyl as defined above, respectively.

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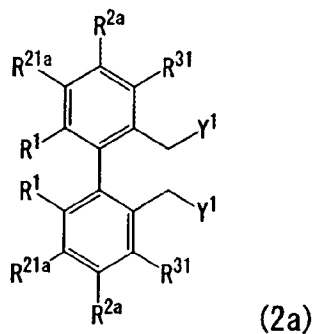
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[0066]



[0067] In the formula,

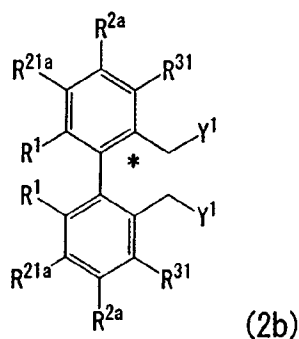
R¹ is the same as above;

R^{2a} and R^{21a} each independently representss halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;

R³¹ represents a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted; and

Y¹ represents a leaving group and preferably represents halogen, a C₁₋₈ alkylsulfonyloxy which is optionally substituted, a C₆₋₁₄ arylsulfonyloxy which is optionally substituted, or a C₇₋₁₆ aralkylsulfonyloxy which is optionally substituted.

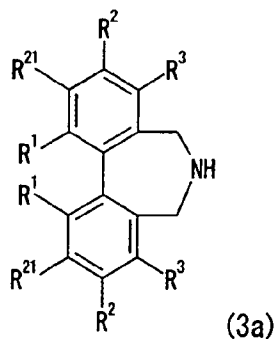
[0068]



[0069] In the formula, R¹, R^{2a}, R^{21a}, R³¹, Y¹, and the symbol * are the same as above.

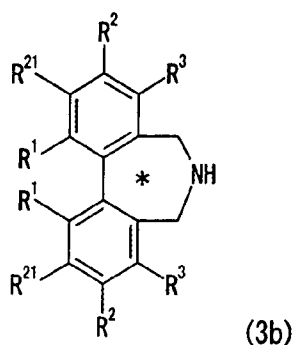
[0070] Examples of the racemic azepine derivative represented by the aforementioned formula (3), which is useful as a production intermediate of the compound represented by the aforementioned formula (1), include the compound represented by the following formula (3a), and examples of the optically active azepine derivative include the compound represented by the following formula (3b).

[0071]



15 **[0072]** In the formula, R^1 , R^2 , R^{21} , and R^3 are the same as above.

[0073]



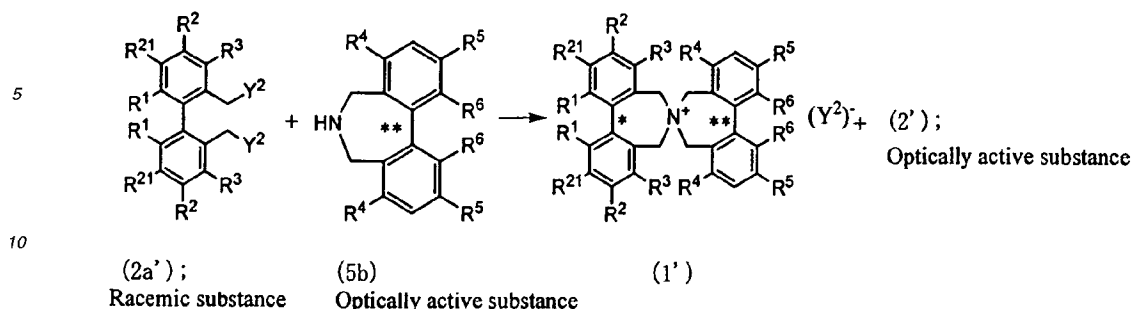
30 **[0074]** In the formula, R^1 , R^2 , R^{21} , R^3 , and the symbol * are the same as above.

35 **[0075]** Since the optically active quaternary ammonium salt compound represented by the aforementioned formula (1) and the following formula (1') (one of the axially asymmetric compounds, which are enantiomeric, is in excess compared to the other) are constituted by an optically active and axially asymmetric biphenyl and optically active and axially asymmetric binaphthyl, or by 2 kinds of optically active and axially asymmetric biphenyl groups, 4 kinds of isomers of said compound exist; i.e., S,S-form, R,R-form, S,R-form, and R,S-form following the conventional symbols showing an axially asymmetric optical activity, and all these isomers are included in the present invention.

40 **[0076]** The quaternary ammonium salt compound (1') of the present invention can be produced, for example, by any one of the following methods.

(i) Reacting a racemic bisbenzyl compound (2a') and optically active azepine derivative (5b)

45 **[0077]**

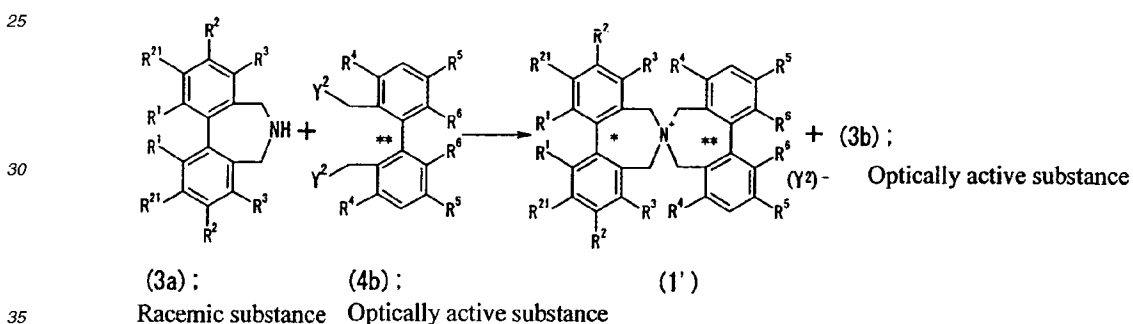


[0078]

(ii) Reacting an optically active bisbenzyl compound (2b') and racemic azepine derivative (5a)
(2b'); optically active substance + (5a); racemic substance → (1') + (5b); optically active substance

(iii) Reacting a racemic azepine derivative (3a) and optically active biphenyl derivative (4b)

[0079]



[0080]

(iv) Reacting an optically active azepine derivative (3b) and racemic biphenyl derivative (4a)
(3b); optically active substance + (4a); racemic substance → (1') + (4b); optically active substance

[0081] In all the production methods (i) to (iv) of the present invention, when optically active materials are reacted with each other, two asymmetric axes of the obtained quaternary ammonium salt compound are both optically active. However, even when one material, which is optically active, is reacted with another material, which is racemic, the former preferentially reacts with one enantiomer of the latter due to kinetic resolution and two asymmetric axes of the obtained quaternary ammonium salt compound are produced so that they are both optically active. For this reason, the enantiomer of the latter material which is not involved in the production is recovered as an optically active substance. Accordingly, in the production method of the present invention, even when one material is not optically active, the quaternary ammonium salt compound having two asymmetric axes which are both optically active can readily be obtained, and thus it is an advantageous method industrially.

[0082] 1 to 10 times of the racemic substance in the present invention can be used relative to the optically active substance in terms of moles, and particularly, the use of 1.5 to 3 times in terms of moles is preferable industrially.

[0083] The present reaction can be carried out under the presence of a solvent or without a solvent. Usable solvents are not particularly limited as long as they are solvents inert to the reaction and examples thereof include hydrocarbon solvents such as pentane, hexane, heptane, benzene, toluene, and xylene; halogen solvents such as dichloromethane, 1,2-dichloroethane, chloroform, and carbon tetrachloride; alcohols such as methanol and ethanol; nitrile solvents such as acetonitrile and propionitrile; ether solvents such as diethylether, dioxane, and tetrahydrofuran; non-protonic polar solvents such as N,N-dimethylformamide and dimethylsulfoxide; water; and mixed solvent systems in which two or more

of these solvents are mixed.

[0084] Examples of the bases include inorganic bases such as sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, sodium bicarbonate, and potassium bicarbonate; and organic bases such as pyridine, triethylamine, N,N-dimethylaniline, 4-dimethylaminopyridine, N-methylpyrrolidine, N-methylmorpholine, and 1,8-diazabicyclo(5.4.0)undeca-7-ene. The amount of base used is normally 1 to 10 times and preferably 1 to 3 times of that of an optically active binaphthyl derivative or optically active biphenyl derivative in terms of moles.

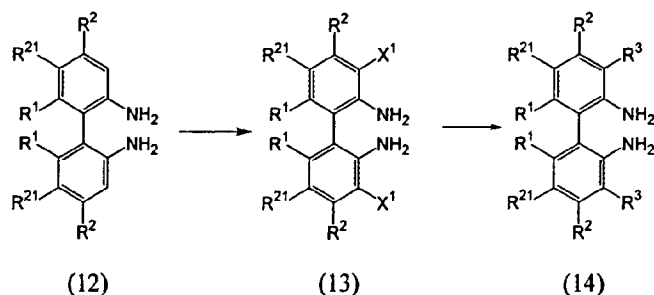
[0085] The temperature range of the present reaction is -78°C to 200°C and preferably -20°C to 100°C . The range of reaction time is 30 minutes to 100 hours, although this depends on the amount of reaction agents, temperature, or the like.

[0086] Bisbenzyl compounds (2a') and (2b') and biphenyl derivatives (4a) and (4b), which are production intermediates, can be produced from the corresponding materials by following the method described in Japanese Laid-Open Patent Application No. 2003-327566, Japanese Laid-Open Patent Application No. 2004-359578, or the like.

[0087] On the other hand, azepine derivatives (3a), (3b), (5a), and (5b), which are production intermediates, can be produced by following the description below.

[0088] That is, 3,3'-dihalogeno-2,2'-dianilines (13), which are obtained by halogenating the bisanilines (12) produced from a known substance based on Japanese Laid-Open Patent Application No. 2004-359578, is reacted under the condition of Suzuki coupling described in Japanese Laid-Open Patent Application No. 2001-48866 or the like (refer to J. Organomet. Chem., 1999, 576, 147) to obtain 3,3'-disubstituted-2,2'-dianilines (14).

[0089]



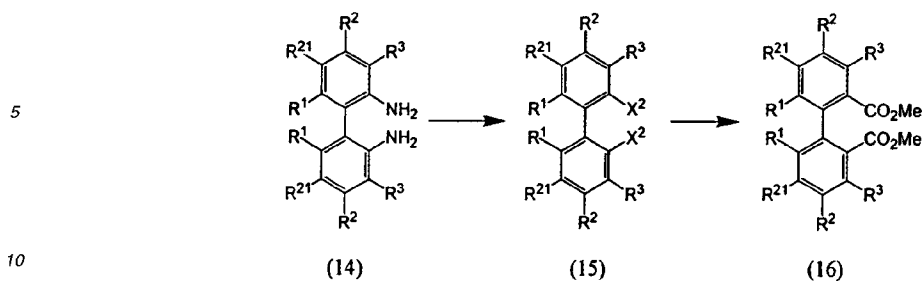
(In the formula, X¹ represents halogen and R¹, R², R²¹, and R³ are the same as above.)

[0090] Examples of the halogenating reagents include N-bromosuccinimide (NBS), N-chlorosuccinimide (NCS), N-iodosuccinimide (NIS), bromine, chlorine, and iodine. Usable solvents are not particularly limited as long as they are solvents inert to the reaction and examples thereof include hydrocarbon solvents such as pentane, hexane, heptane, benzene, toluene, and xylene; halogen solvents such as dichloromethane, 1,2-dichloroethane, chloroform, and carbon tetrachloride; alcohols such as methanol and ethanol; and mixed solvent systems in which two or more of these solvents are mixed. The reaction can be carried out at an appropriate temperature from room temperature to the boiling point of the solvent.

[0091] Subsequently, a 3,3'-disubstituted-2,2'-dihalogenated substance (15) is prepared by converting the amino group in 3,3'-disubstituted-2,2'-dianilines (14) to halogen using a nitrite, and by treating this substance (15) with a carbon monoxide-Pd catalyst, a 3,3'-disubstituted-2,2'-diester substance (16) is obtained.

[0092] The conversion of amino to halogen due to a nitrite can be carried out based on the method described in Japanese Laid-Open Patent Application No. 2004-359578, and the conversion of the 3,3'-disubstituted-2,2'-dihalogenated substance (15) to the 3,3'-disubstituted-2,2'-diester substance (16) can be carried out based on the method described in Synlett (1998) 2, 183.

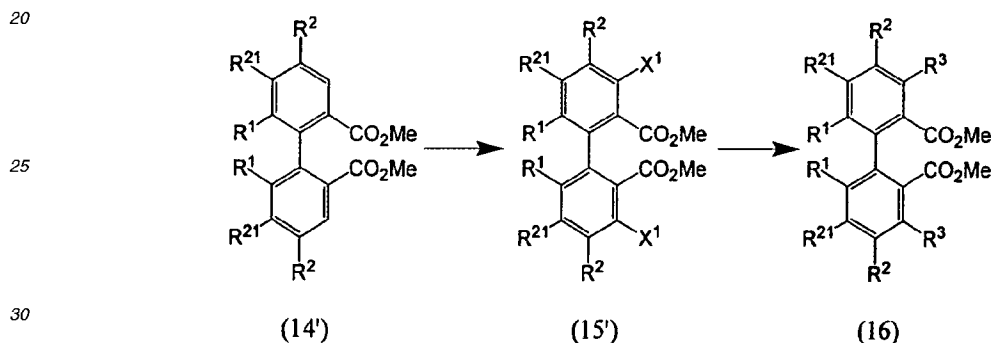
[0093]



(In the formula, X² represents halogen and R¹, R², R²¹, and R³ are the same as above.)

15 [0094] Moreover, by carrying out halogenation/Suzuki coupling reaction due to the method according to the above using a known compound or a biphenyl-2,2'-diester substance (14'), which can be derived by known methods, 3,3'-disubstituted-2,2'-diester substance (16) can also be obtained via 3,3'-dihalo derivative (15').

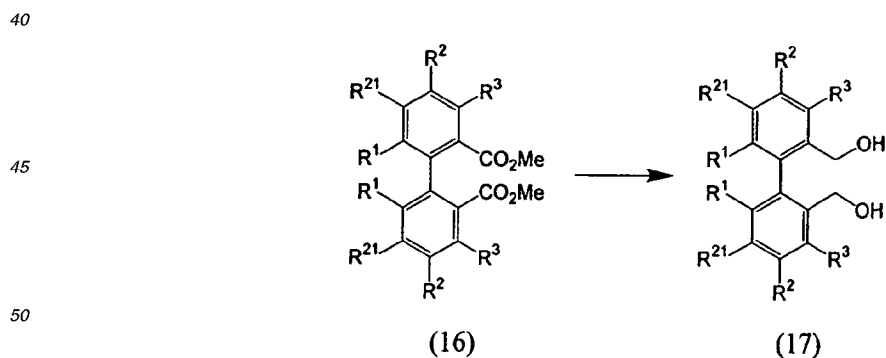
[0095]



(In the formula, X¹, R¹, R², R²¹, and R³ are the same as above.)

35 [0096] 3,3'-disubstituted-2,2'-bishydroxymethyl substance (17) can be obtained by reducing 3,3'-disubstituted-2,2'-diester substance (16) due to the method described in Jikken Kagaku Koza (Courses in Experimental Chemistry, 4th Ed., edited by The Chemical Society of Japan and published by Maruzen Co., Ltd., vol. 20, pp.10-141).

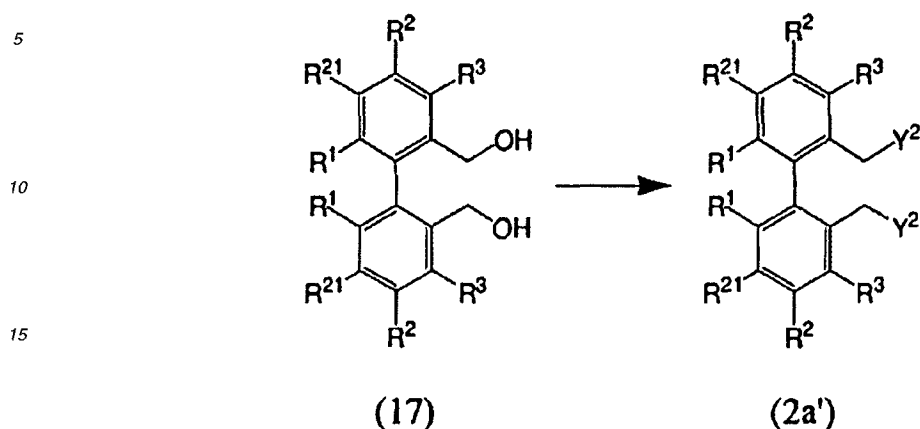
[0097]



(In the formula, R¹, R², R²¹, and R³ are the same as above.)

55 [0098] Subsequently, the hydroxyl in 3,3'-disubstituted-2,2'-bishydroxymethyl substance (17) is converted to a leaving group such as halogen based on the method described in Jikken Kagaku Koza (Courses in Experimental Chemistry, 4th Ed., edited by The Chemical Society of Japan and published by Maruzen Co., Ltd., vol. 19, pp.438-445) to obtain a bisbenzyl compound (2a').

[0099]



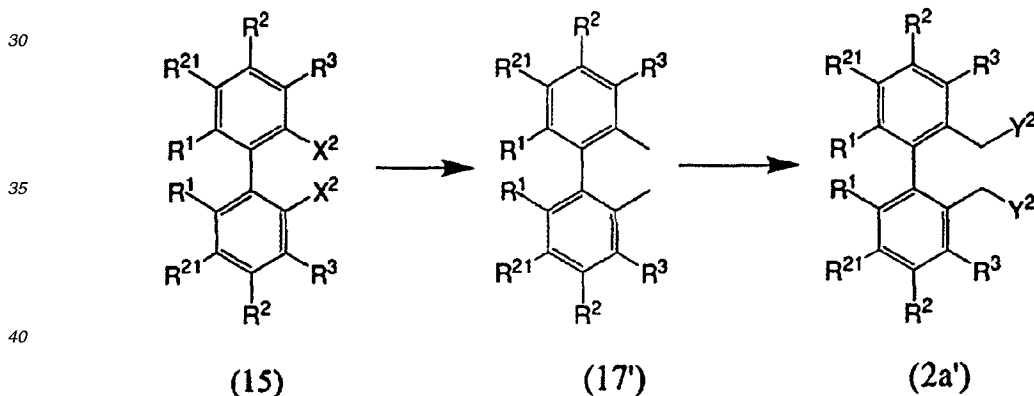
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[0100] (In the formula, Y² represents a leaving group and R¹, R², R²¹, and R³ are the same as above.)

Examples of the abovementioned leaving group Y² include halogen, p-toluenesulfonyloxy, and methanesulfonyloxy.

25 [0101] On the other hand, 3,3'-disubstituted-2,2'-dihalogen substance (15) can be converted to 3,3'-disubstituted-2,2'-dimethyl substance (17') according to the method described in a document (J. Mol. Catal., 1990, 60, 343), and the bisbenzyl compound (2a') can also be obtained by subjecting the substance (17') to a general halogenation condition.

[0102]

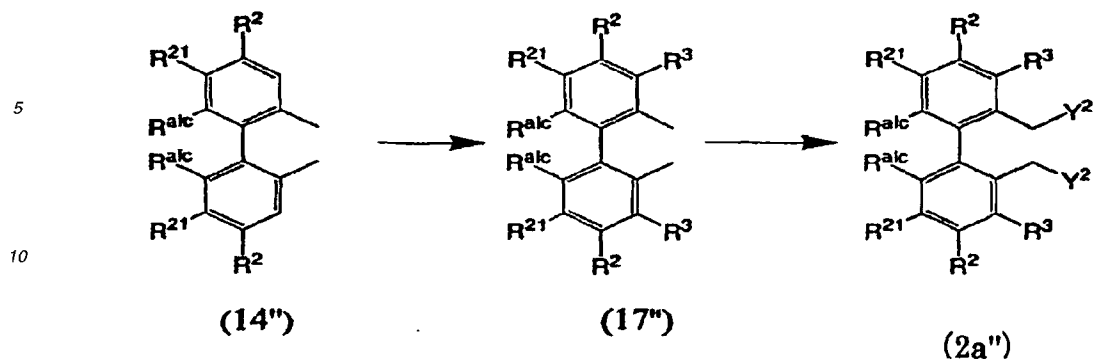


45 (In the formula, R¹, R², R²¹, R³, and Y² are the same as above.)

[0103] Furthermore, 6,6'-dialkoxy-3,3'-disubstituted-2,2'-dimethyl substance (17'') is obtained, for example, by carrying out halogenation/Suzuki coupling reaction according to the aforementioned method using 6,6'-dialkoxy-2,2'-dimethyl-biphenyl derivative (14''), which can be synthesized based on a document (J. Chem. Soc., 1950, 711) or the like. By the same treatment carried out on the substance (17') to prepare the substance (2a'), the substance (17'') can be derived to a corresponding bisbenzyl compound (2a'').

[0104]

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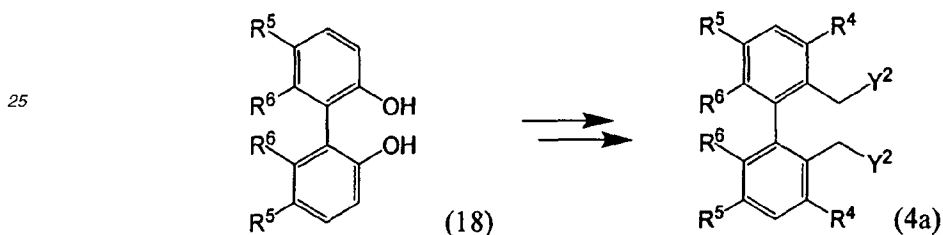
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[0105] (In the formula, R^{alc} represents alkoxy and R², R³, R²¹, and Y² are the same as above.)

[0106] In addition, it is possible to obtain biphenyl derivatives (4a) from diols (18) according to a document (J. Am. Chem. Soc., 121, 6519 (1999)).

[0107]

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[0108] (In the formula, R⁴, R⁵, R⁶, and Y² are the same as above.)

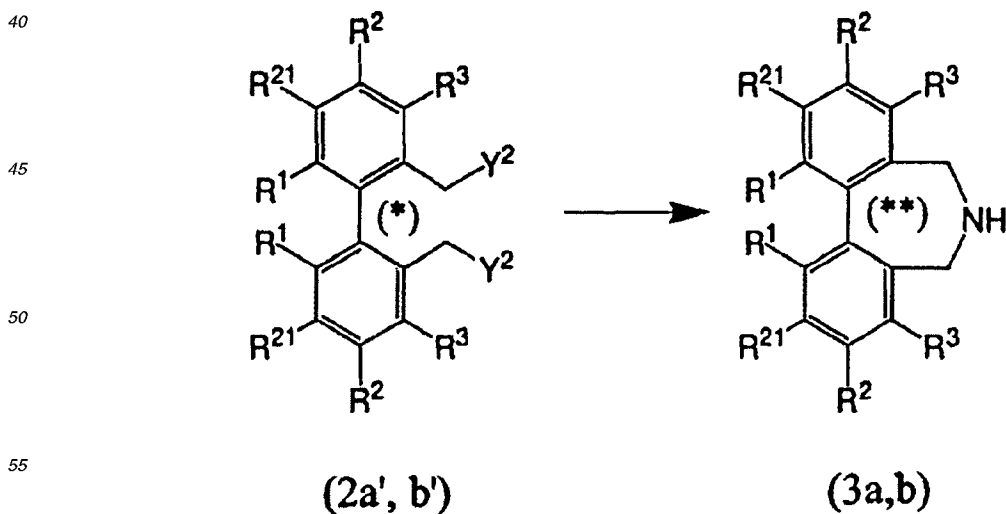
[0109] The synthesis method of the aforementioned bisbenzyl compound (2a') and biphenyl derivatives (4a) can be applied to the corresponding optically-active compounds (2b') and (4b).

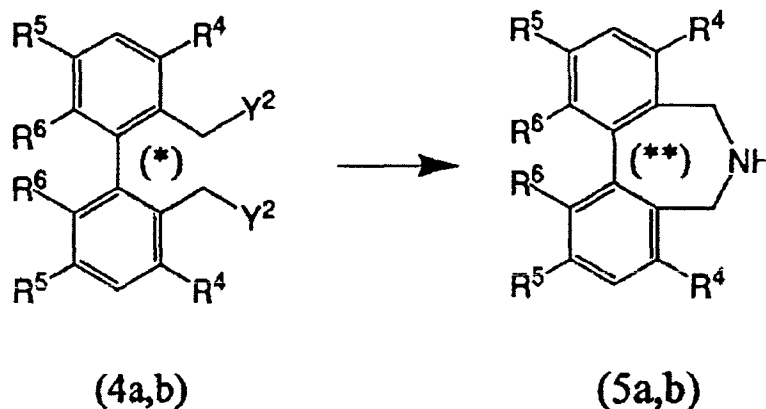
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[0110] By reacting these biphenyls with ammonia, an azepine derivative (3a), (3b), (5a), or (5b) can be produced.

[0111]

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[0112] (In the formula, R¹, R², R²¹, R³, R⁴, R⁵, R⁶, X, and X³ are the same as above and the symbols (*) and (**) represents optical activity when the compound is labeled with the alphabet "b".)

[0113] The present reaction can be carried out by reacting the respective solvent solutions of biphenyls and ammonia, or by reacting one with the other's solvent solution directly.

Although the solvent used is not particularly limited as long as it does not react with biphenyls and ammonia, examples thereof include hydrocarbon solvents such as pentane, hexane, heptane, benzene, toluene, and xylene; halogen solvents such as dichloromethane, 1,2-dichloroethane, chloroform, and carbon tetrachloride; alcohols such as methanol and ethanol; nitrile solvents such as acetonitrile and propionitrile; ether solvents such as diethylether, dioxane, and tetrahydrofuran; non-protonic polar solvents such as N,N-dimethylformamide and dimethylsulfoxide; water; and mixed solvent systems in which two or more of these solvents are mixed. In addition, the solvent for dissolving ammonia is not particularly limited as long as it does not react with ammonia. Examples thereof include hydrocarbon solvents such as pentane, hexane, heptane, benzene, toluene, and xylene; halogen solvents such as dichloromethane, 1,2-dichloroethane, chloroform, and carbon tetrachloride; alcohols such as methanol and ethanol; nitrile solvents such as acetonitrile and propionitrile; ether solvents such as diethylether, dioxane, and tetrahydrofuran; non-protonic polar solvents such as N,N-dimethylformamide and dimethylsulfoxide; water; and mixed solvent systems in which two or more of these solvents are mixed.

[0114] Although the method is not particularly limited, the reaction can be carried out, for example, by adding ammonia, in either gaseous form or liquid form, to the solution of biphenyls directly, or by adding the aforementioned solvent solution of ammonia dropwise to the solution of biphenyls.

Although the mixing ratio of a solvent and biphenyls is not particularly limited, it can appropriately be set from 1: 1 to 100: 1 (volume: weight). Likewise, ammonia can also be used in an arbitrary concentration.

The mole ratio of biphenyls and ammonia is from 1: 0.2 to 1: 10 and preferably from 1: 1 to 1: 5.

Reaction temperature is -70°C to the boiling point of solvents and preferably -20°C to 40°C.

[0115] After completing the reaction and the distillation process to remove unreacted ammonia, azepine derivatives can be separated/purified by applying known conventional methods such as extraction, washing, distillation, column chromatography, drying, and recrystallization.

[0116] The production of an optically active quaternary ammonium salt compound (1) can be carried out by following the condition of a general N-benylation reaction as shown below.

- (a) Reacting an optically active bisbenzyl compound (2b') with an optically active azepine derivative (5b); or
- (b) Reacting an optically active biphenyl compound (4b) with an optically active azepine derivative (3b)

[0117] Additionally, the production of an optically active quaternary ammonium salt compound (1) can also be carried out by the kinetic resolution method. In other words, it can be performed by reacting a racemic substance with an optically active substance as shown below.

- (i) Reacting a racemic bisbenzyl compound (2a') with an optically active azepine derivative (5b);
- (ii) Reacting an optically active bisbenzyl compound (2b') with a racemic azepine derivative (5a);
- (iii) Reacting a racemic azepine derivative (3a) with an optically active biphenyl derivative (4b); or
- (iv) Reacting an optically active azepine derivative (3b) with a racemic biphenyl derivative (4a)

[0118] The reaction between 2 kinds of the aforementioned substances can readily be carried out in an appropriate solvent under the presence of a base.

[0119] Solvents can be used regardless of their type as long as they are not involved in the reaction. Examples thereof include hydrocarbon solvents such as pentane, hexane, heptane, benzene, toluene, and xylene; halogen solvents such as dichloromethane, 1,2-dichloroethane, chloroform, and carbon tetrachloride; alcohols such as methanol and ethanol; nitrile solvents such as acetonitrile and propionitrile; ether solvents such as diethylether, dioxane, and tetrahydrofuran; non-protonic polar solvents such as N,N-dimethylformamide and dimethylsulfoxide; and mixed solvent systems in which two or more of these solvents are mixed. However, since the present reaction can be carried out under the phase-transfer reaction conditions, solvent systems, in which a water-insoluble solvent among the aforementioned solvents and water are combined, can also be used.

[0120] Although general inorganic bases can be used as the base, which may be used, more preferable examples thereof include sodium hydroxide, potassium hydroxide, sodium carbonate, and potassium carbonate.

[0121] Reaction can be performed in a solvent or in a solvent system while stirring under the presence of a base, and in a temperature range from the solidifying point to the boiling point of the solvent or the solvent system. Reaction temperature is preferably -20°C to 80°C. Although reaction time can be adjusted appropriately depending on the reaction temperature, reactions can be completed in 30 minutes to 12 hours.

[0122] The volume of the abovementioned reaction solvent is 1 to 100 times larger and more preferably 5 to 50 times larger in terms of volume (ml)/ weight (g) ratio with respect to the total weight of the 2 substances.

[0123] Although the charged mole ratio of the aforementioned 2 substances is preferably 1: 1 when the condition is for a general N-benylation reaction, more favorable results can be obtained by increasing the amount of one substance, which is more readily available than the other. When using the kinetic resolution method, the ratio of an optically active substance and racemic substance is preferably 1: 2 to 1: 5 and more preferably 1: 2 to 1: 3.

[0124] The amount of base used is preferably 1 to 6 equivalent and more preferably 1 to 3 equivalent of the leaving group Y², which is present in the reaction system, when the condition is for a general N-benylation reaction. When using the kinetic resolution method, the amount of base used is preferably 1 to 6 equivalent and more preferably 1 to 3 equivalent of the leaving group Y², which is present in the reaction system, if an azepine derivative is an optically active substance, and the amount of base used is preferably 0 to 4 equivalent and more preferably 0 to 1 equivalent of the leaving group Y², which is present in the reaction system, if the azepine derivative is a racemic substance.

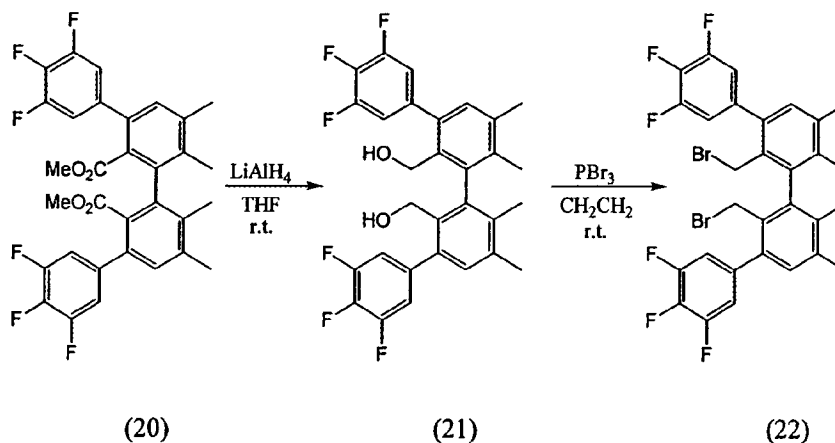
[0125] The compound (1) which is produced as such can provide a reaction product having a high optical purity when used as a phase transfer catalyst in the asymmetric alkylation of an α-amino acid derivative.

[0126] Although the present invention will be described in more detail below using Examples and Reference Examples, the technical scope of the present invention is not limited to these Examples.

Example 1

[0127] Production of 2',2"-bis(bromomethyl)-3,4,5,3'',4'',5''-hexafluoro-4',5',4'',5''-tetramethyl-(1,1';3',3' ;1'',1''') quaterphenyl (22)

[0128]



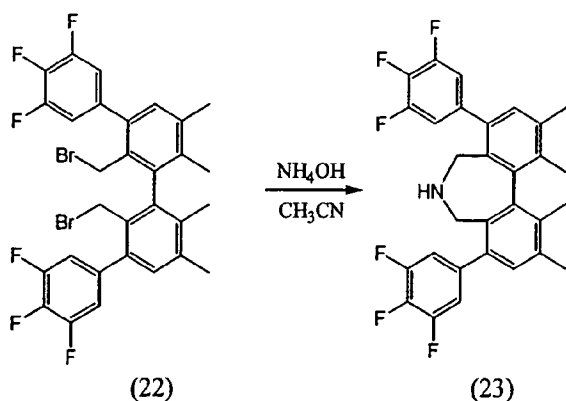
[0129] After dissolving 156 mg (0.27 mmol) of a compound (20) in 5 ml of THF and cooling the resultant down to 0°C,

31 mg (0.81 mmol) of LiAlH_4 was added thereto. After increasing the temperature of the mixture slowly to room temperature, the mixture was further stirred for 5 hours. Thereafter, the reaction was stopped by pouring the reaction solution into ice-cold water, and an alcoholic substance (21) was obtained by carrying out further procedures of extraction/drying/concentration. Without subjecting to further purification procedures, the alcoholic substance (21) was dissolved in 5 ml of CH_2Cl_2 , and 0.26 ml (0.6 mmol) of PBr_3 was added dropwise to the resulting solution at 0°C . After stirring for 2 hours at room temperature, the reaction solution was poured into ice-cold water to stop the reaction. The reaction solution was then further extracted using methylene chloride and the resultant was dried/concentrated and thereafter purified by column chromatography (ethyl acetate: hexane = 1: 10) to obtain 137 mg (0.21 mmol) of a compound (22) (yield was 77%).

^1H NMR (300MHz, CDCl_3), δ 7.15 (2H, d, $J=6.6\text{Hz}$, ArH), 7.12 (2H, d, $J=6.6\text{Hz}$, ArH), 7.09 (2H, s, ArH), 4.03 (4H, d, $J=2.4\text{Hz}$, ArCH_2), 2.37 (6H, s, ArCH_3), 1.97 (6H, s, ArCH_3)

Example 2

[0130] Production of 1,2,10,11-tetramethyl-4,8-bis(3,4,5-trifluorophenyl)-6,7-dihydro-5H-dibenzo(c,e)azepine
[0131]

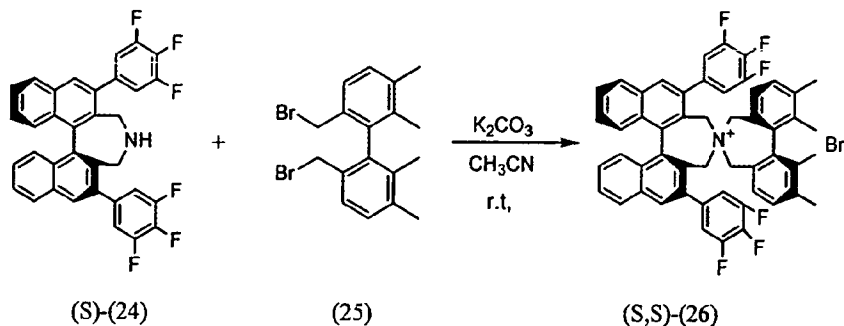


[0132] 65 mg (0.1 mmol) of the compound (22) and 0.2 ml of 25% ammonia water were stirred in an acetonitrile solvent at room temperature for 24 hours. After the completion of the reaction, the resultant was extracted/dried/concentrated, and thereafter purified by column chromatography (methanol: methylene chloride = 1: 10) to obtain 51 mg (0.1 mmol) of a compound (23) (yield was 100%).

^1H NMR (300MHz, CD_3OD), δ 7.31 (2H, s, ArH), 7.24 (2H, d, $J=6.6\text{Hz}$, ArH), 7.21 (2H, d, $J=6.6\text{Hz}$, ArH), 4.14 (2H, d, $J=13.8\text{Hz}$, ArCH_2), 3.46 (2H, d, $J=13.8\text{Hz}$, ArCH_2), 2.43 (6H, s, ArCH_3), 2.09 (6H, s, ArCH_3)

Example 3

[0133] Production of optically active quaternary ammonium salt compound (26) (homo)
[0134]



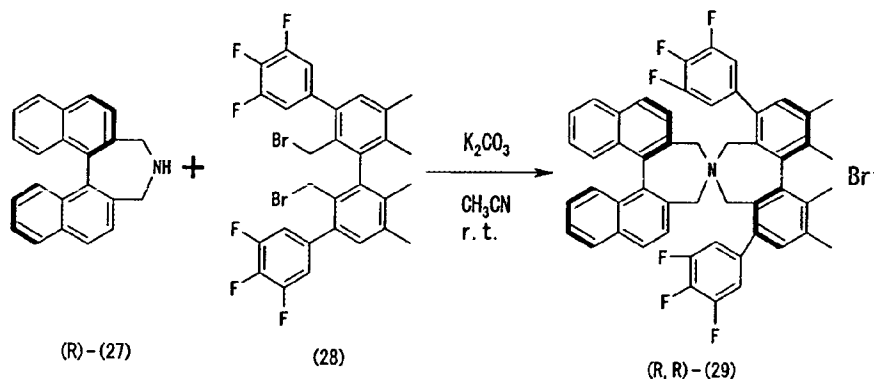
[0135] Under the presence of 140 mg of potassium carbonate, 56 mg of a chiral secondary amine (24) and 80 mg of racemic dibromomethylbiphenyl (25), which was 2.1 equivalent of said amine, were stirred in an acetonitrile solvent at room temperature for 12 hours. After the completion of the reaction, the resultant was purified by extraction/column chromatography (methylene chloride: methanol = 10: 1) to obtain 74 mg of an optically pure compound (S, S)-(26) (yield was 85%). $[\alpha]_D^{22} = +25.6^\circ$ (c1.0, CHCl_3)

$^1\text{H NMR}$ (300MHz, CDCl_3), δ 8.21 (2H, s, ArH), 8.08 (2H, d, $J=8.4\text{Hz}$, ArH), 7.205-7.60 (8H, m, ArH), 7.09 (2H, d, $J=8.7\text{Hz}$, ArH), 6.71 (2H, d, $J=7.8\text{Hz}$, ArH), 6.02 (2H, d, $J=7.8\text{Hz}$, ArH), 4.71 (2H, d, $J=13.8\text{Hz}$, ArCH_2), 4.50 (2H, d, $J=14.1\text{Hz}$, ArCH_2), 4.04 (2H, d, $J=13.5\text{Hz}$, ArCH_2), 3.49 (2H, d, $J=13.2\text{Hz}$, ArCH_2), 2.30 (6H, s, ArCH_3), 1.88 (6H, s, ArCH_3)

Example 4

[0136] Production of optically active quaternary ammonium salt compound (29) (homo)

[0137]



[0138] Under the presence of 140 mg of potassium carbonate, 56 mg of a chiral secondary amine (27) and 80 mg of racemic dibromomethylbiphenyl (28), which was 2.1 equivalent of said amine, were stirred in an acetonitrile solvent at room temperature for 12 hours as in Example 1. After the completion of the reaction, the resultant was purified by extraction/column chromatography (methylene chloride: methanol = 10: 1) to obtain 82 mg of an optically pure compound (R, R)-(29) (yield was 94%).

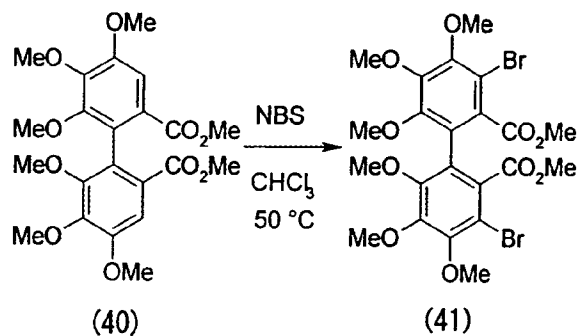
$[\alpha]_D^{23} = -120.2^\circ$ (c1.0, CHCl_3)

$^1\text{H NMR}$ (300MHz, CDCl_3), δ 7.92 (2H, d, $J=8.4\text{Hz}$, ArH), 7.20-7.57 (12H, m, ArH), 7.11 (2H, d, $J=8.4\text{Hz}$, ArH), 6.32 (2H, d, $J=8.7\text{Hz}$, ArH), 4.55 (2H, d, $J=13.8\text{Hz}$, ArCH_2), 4.47 (4H, d, $J=14.1\text{Hz}$, ArCH_2), 4.18 (2H, d, $J=14.1\text{Hz}$, ArCH_2), 3.61 (2H, d, $J=12.9\text{Hz}$, ArCH_2), 2.45 (6H, s, ArCH_3), 2.05 (6H, s, ArCH_3)

Example 5

[0139] Production of optically active quaternary ammonium salt compound (45)

[0140]

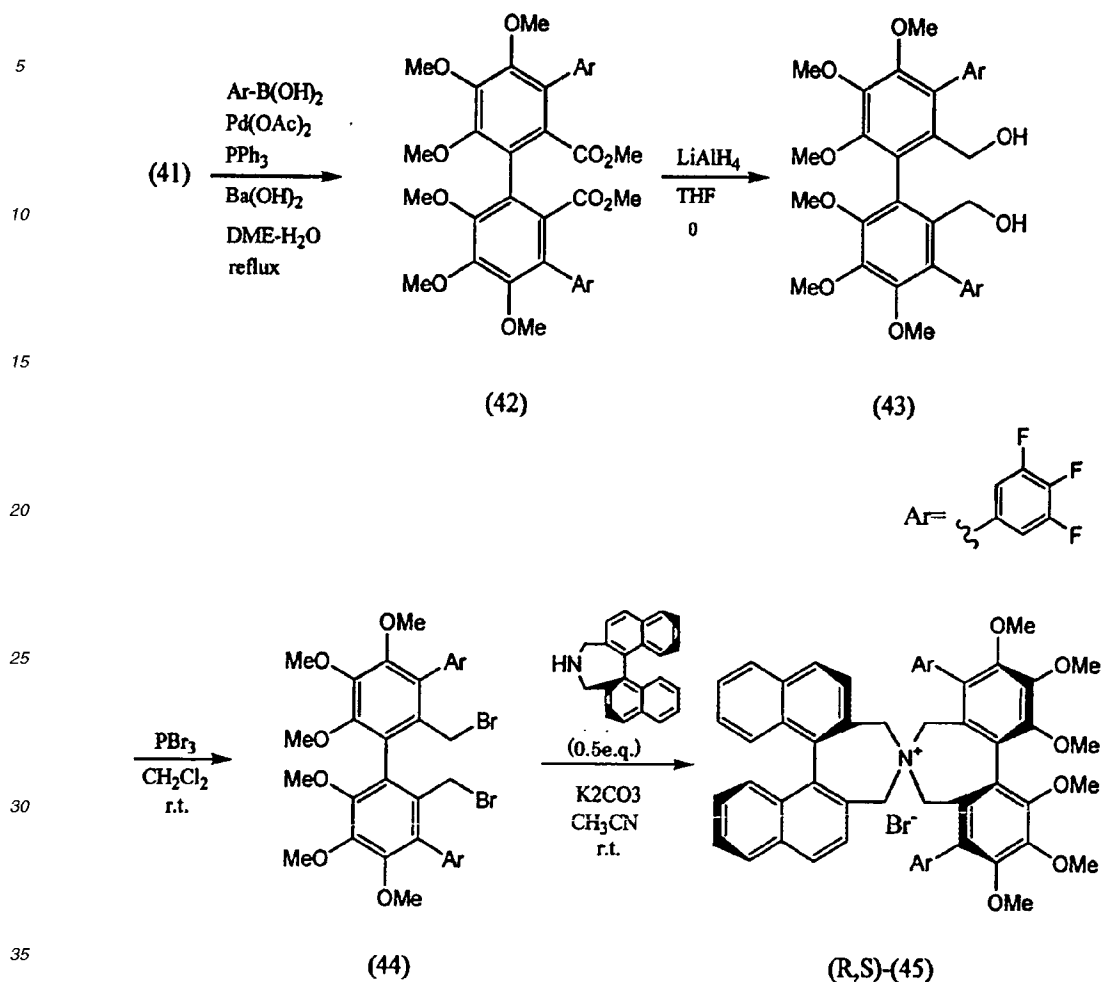


[0141] 1.97 g (4.37 mmol) of a compound (40) and 2.33 g (13.1 mmol) of N-bromosuccinimide were reacted in 20 ml of a chloroform solvent at room temperature for 12 hours. After the completion of the reaction, the resultant was extracted with ethyl acetate, dried/concentrated, and thereafter purified by column chromatography (ethyl acetate: hexane = 1: 3) to obtain a compound (41) (yield was 94%).

¹H NMR (300MHz, CDCl₃), δ3.96 (6H, s, ArCO₂CH₃), 3.94 (6H, s, ArOCH₃), 3.79 (6H, s, ArOCH₃), 3.94 (6H, s, ArOCH₃)

[0142] The compounds (41) to (45) were synthesized according to the methods of Reference Example 7, and Examples 1 and 4.

[0143]



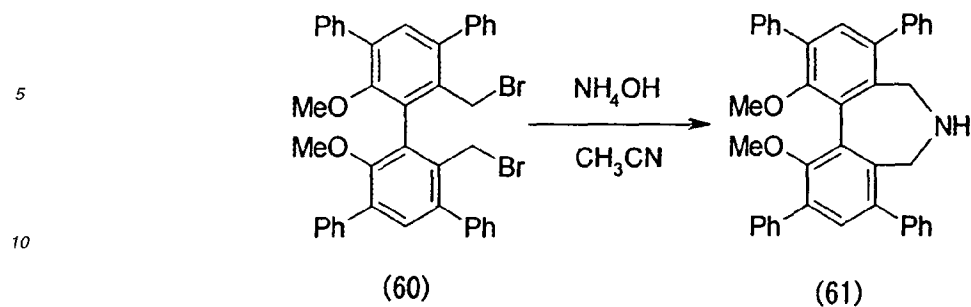
[0144] Compound (42) (yield was 80%)
¹H NMR (300MHz, CDCl₃), δ6.90-6.95 (4H, m, ArH), 3.98 (6H, s, ArCO₂CH₃), 3.85 (6H, s, ArOCH₃), 3.70 (6H, s, ArOCH₃), 3.27 (6H, s, ArOCH₃)

[0145] Compound (44) (yield was 81% from the compound (42))
¹H NMR (300MHz, CDCl₃), δ6.95-7.15 (4H, m, ArH), 3.90-4.00 (4H, m, ArCH₂O-), 3.95 (6H, s, ArOCH₃), 3.87 (6H, s, ArOCH₃), 3.73 (6H, s, ArOCH₃)

Compound (45) (yield was 83%)
 [α]_D²² = -89.55° (c0.22, CHCl₃)
¹H NMR (300MHz, CDCl₃), δ6.75-8.00 (12H, m, ArH), 6.47 (4H, d, J=8.4Hz, ArH), 4.65 (2H, d, J=14.1Hz, ArCH₂), 4.44 (2H, d, J=12.6Hz, ArCH₂), 4.40 (2H, d, J=13.5Hz, ArCH₂), 4.11 (6H, s, ArOCH₃), 3.91 (6H, s, ArOCH₃), 3.75 (6H, s, ArOCH₃), 3.61 (2H, d, J=13.8Hz, ArCH₂)

Example 6

[0146]



15 Production of amine (61)

[0147] 30 mg (0.043 mmol) of a compound (60) was dissolved in 2 ml of acetonitrile, and 0.1 to 0.2 ml of 25% ammonia water solution was added dropwise thereto. The reaction mixture was stirred at room temperature for 48 hours, concentrated to remove the solvent, and extracted with ethyl acetate. The resultant was subjected to drying/concentration and thereafter purified by column chromatography (methylene chloride: methanol = 15: 1) to obtain 20 mg (0.036 mmol) of a targeted substance (61) (yield was 84%).

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[0148] The compounds of the present invention including those obtained in the abovementioned Examples are described in Tables 1 to 4.

[0149]

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Optically active quaternary ammonium salt (1)

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(continued)

Compound No.	R ¹	R ²	R ²¹	R ³	R ⁴	x	Physical property value (¹ HNMR, 300MHz, CDCl ₃)	Physical property (angle of rotation)	Note
29	Me	H	Me	3,4,5-F ₃ -C ₆ H ₂	H	Br	δ 7.92 (2H, d, J=8.4Hz, ArH), 7.20-7.57 (12H, m, ArH), 7.11 (2H, d, J=8.4Hz, ArH), 6.32 (2H, d, Jm8.7Hz, ArH), 4.55 (2H, d, J=13.8Hz, ArCH ₂), 4.47 (4H, d, J=14.1Hz, ArCH ₂), 4.18 (2H, d, J=14.1Hz, ArCH ₂), 3.61 (2H, d, J=12.9Hz, ArCH ₂), 2.45 (6H, s, ArCH ₃), 2.05 (6H, s, ArCH ₃)	[α] _D ²³ = -120.2° (c1.0, CHCl ₃)	R, R-form
30	Me	H	Me	H	3,5-(CF ₃) ₂ -C ₆ H ₂	Br	δ 8.27 (2H, s, ArH), 7.35-8.16 (12H, m, ArH), 7.16 (2H, d, J=8.7Hz, ArH), 6.43 (2H, d, J=7.8Hz, ArH), 5.73 (2H, d, J=7.8Hz, ArH), 4.71 (2H, d, J=14.1Hz, ArCH ₂), 4.53 (2H, d, J=13.8Hz, ArCH ₂), 4.10 (2H, d, J=13.5Hz, ArCH ₂), 3.42 (2H, d, J=12.9Hz, ArCH ₂), 2.20 (6H, s, ArCH ₃), 1.82 (6H, s, ArCH ₃)	[α] _D ²² = +25.6° (c1.0, CHCl ₃)	S, S-form

(continued)

Compound No.	R ¹	R ²	R ²¹	R ³	R ⁴	x	Physical property value (¹ HNMR, 300MHz, CDCl ₃)	Physical property (angle of rotation)	Note
31	Me	H	Me	H	3,4,5-F ₃ -C ₆ H ₂	Br	δ8.22 (2H, s, ArH), 8.08 (2H, d, J=8.4Hz, ArH), 7.84 (2H, d, J=7.2Hz, ArH), 6.91-7.60 (12H, m, ArH), 5.90 (2H, d, J=7.5Hz, ArH), 4.85 (2H, d, J=14.1Hz, ArCH ₂), 4.57 (2H, d, J=13.5Hz, ArCH ₂), 4.11 (2H, d, J=13.5Hz, ArCH ₂), 3.76 (6H, s, OCH ₃), 3.61 (2H, d, J=12.9Hz, ArCH ₂)	[α] _D ²³ =+18.0° (c0.15, CHCl ₃)	S, R-form
45	OMe	OMe	OMe	3,4,5-F ₃ -C ₆ H ₂	H	Br	δ6.75-8.00 (12H, m, ArH), 6.47 (4H, d, J=8.4Hz, ArH), 4.65 (2H, d, J=14.1Hz, ArCH ₂), 4.44 (2H, d, J=12.6Hz, ArCH ₂), 4.40 (2H, d, J=13.5Hz, ArCH ₂), 4.11 (6H, s, ArOCH ₃), 3.91 (6H, s, ArOCH ₃), 3.75 (6H, s, ArOCH ₃), 3.61 (2H, d, J=13.8Hz, ArCH ₂)	[α] _D ²² =-89.55° (c0.22, CHCl ₃)	R, S-form

(continued)

Compound No.	R ¹	R ²	R ²¹	R ³	R ⁴	x	Physical property value (¹ HNMR, 300MHz, CDCl ₃)	Physical property (angle of rotation)	Note
46	OMe	OMe	OMe	H	3,5-(CF ₃) ₂ -C ₆ H ₂	Br	δ8.76 (2H, s, ArH), 8.17 (2H, s, ArH), 7.01-7.92 (12H, m, ArH), 6.11 (2H, d, J=8.4Hz, ArH), 2.25-4.80 (8H, m, ArCH ₂), 4.14 (4H, s, ArOCH ₃ , homo), 4.09 (2H, s, ArOCH ₃ , hetero), 4.07 (2H, s, ArOCH ₃ , hetero), 3.98 (4H, s, ArOCH ₃ , homo), 3.81 (2H, s, ArOCH ₃ , hetero), 3.76 (4H, s, ArOCH ₃ , homo)	[α] _D ²² =-63.125° (c0.48, CHCl ₃)	Mixture of R,S-form and R,R-form (ratio is 2: 1)
47	OMe	H	C ₆ H ₅	C ₆ H ₅	H	Br	87.08-7.85 (32H, m, ArH), 6.15 (2H, d, J=8.4Hz, ArH), 4.86 (2H, d, J=13.8Hz, ArCH ₂), 4.69 (2H, d, J=13.5Hz, ArCH ₂), 4.38 (2H, d, J=13.2Hz, ArCH ₂), 3.69 (2H, d, J=13.2Hz, ArCH ₂), 3.43 (6H, s, ArOCH ₃)		

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Compound No.	R ¹	R ²	R ²¹	R ³	R ⁴	x	Physical property value (¹ HNMR, 300MHz, CDCl ₃)	Physical property (angle of rotation)	Note
48	OMe	H	4-CF ₃ -C ₆ H ₄	4-CF ₃ -C ₆ H ₄	H	Br	δ7.07-7.95 (28H, m, ArH), 6.11 (2H, d, J=8.4Hz, ArH), 4.90 (2H, d, J=12.0Hz, ArCH ₂), 4.74 (2H, d, J=13.8Hz, ArCH ₂), 4.46 (2H, d, J=14.7Hz, ArCH ₂), 3.69 (2H, d, J=13.8Hz, ArCH ₂), 3.44 (6H, s, ArOCH ₃)		
49	OMe	H	4-F-C ₆ H ₄	4-F-C ₆ H ₄	H	Br	7.60-7.65 (4H, m, ArH), 7.40-7.55 (4H, m, ArH), 7.28 (2H, s, ArH), 7.05-7.20 (8H, m, ArH), 4.27 (4H, s, ArCH ₂), 3.35 (6H, s, ArOCH ₃)		
50	OMe	H	3-CF ₃ -C ₆ H ₄	3-CF ₃ -C ₆ H ₄	H	Br	87.02-7.98 (28H, m, ArH), 6.14 (2H, br, ArH), 4.71 (2H, d, J=13.2Hz, ArCH ₂), 3.40-3.77 (6H, m, ArCH ₂), 3.55 (6H, s, ArOCH ₃)		

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Compound No.	R ¹	R ²	R ²¹	R ³	R ⁴	x	Physical property value (¹ HNMR, 300MHz, CDCl ₃)	Physical property (angle of rotation)	Note
51	OMe	H	3,5-CF ₃ -C ₆ H ₃	3,5-CF ₃ -C ₆ H ₃	H	Br	δ7.05-8.22 (24H, m, ArH), 6.00 (2H, d, J=8.4Hz, ArH), 5.11 (2H, br, ArCH ₂), 4.51-4.60 (4H, m, ArCH ₂), 3.73 (2H, d, J=13.2Hz, ArCH ₂), 3.52 (6H, s, ArOCH ₃)		
52	OMe	OMe	H	3,5-CF ₃ -C ₆ H ₃	H	Br	δ8.75 (2H, s, ArH), 8.10 (2H, s, ArH), 6.85-7.93 (14H, m, ArH), 6.22 (2H, d, J=8.4Hz, ArH), 4.55 (2H, d, J=13.5Hz, ArCH ₂), 4.43 (2H, d, J=13.5Hz, ArCH ₂), 4.31 (2H, d, J=13.5Hz, ArCH ₂), 3.99 (12H, s, ArOCH ₃), 3.58 (2H, d, J=13.5Hz, ArCH ₂)		
53	OMe	H	OMe	3,5-CF ₃ -C ₆ H ₃	H	Br	δ8.22 (2H, s, ArH), 6.98-7.95 (16H, m, ArH), 5.95 (2H, d, J=8.4Hz, ArH), 4.66 (2H, d, J=12.9Hz, ArCH ₂), 4.32-4.42 (4H, m, ArCH ₂), 4.11 (6H, s, ArOCH ₃), 3.94 (6H, s, ArOCH ₃), 3.57 (2H, d, J=13.5Hz, ArCH ₂)		

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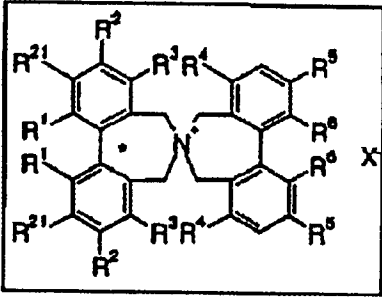
Compound No.	R ¹	R ²	R ²¹	R ³	R ⁴	x	Physical property value (¹ HNMR, 300MHz, CDCl ₃)	Physical property (angle of rotation)	Note
54	OMe	H	H	3,5-CF ₃ -C ₆ H ₃	H	Br	δ8.18 (2H, s, ArH), 7.03-7.95 (18H, m, ArH), 6.04 (2H, d, J=8.4Hz, ArH), 4.66 (2H, d, J=14.1Hz, ArCH ₂), 4.50 (2H, d, J=13.5Hz, ArCH ₂), 4.45 (2H, d, J=13.8Hz, ArCH ₂), 3.94 (6H, s, ArOCH ₃), 3.63 (2H, d, J=13.2Hz, ArCH ₂)		
55	OMe	H	H	3,4,5-F ₃ -4C ₆ H ₂	H	Br	δ7.92 (2H, d, J=8.4Hz, ArH), 7.09-7.65 (16H, m, ArH), 6.35 (2H, d, J=8.4Hz, ArH), 4.62 (2H, d, J=13.8Hz, ArCH ₂), 4.45-4.52 (4H, m, ArCH ₂), 3.89 (6H, s, ArOCH ₃), 3.68 (2H, d, J=13.5Hz, ArCH ₂)		

(continued)

Compound No.	R ¹	R ²	R ²¹	R ³	R ⁴	x	Physical property value (¹ HNMR, 300MHz, CDCl ₃)	Physical property (angle of rotation)	Note
56	OMe	OMe	OMe	3,5-CF ₃ -C ₆ H ₃	H		δ6.75-8.00 (12H, m, ArH), 6.47 (4H, d, J=8.4Hz, ArH), 4.65 (2H, d, J=14.1Hz, ArCH ₂), 4.44 (2H, d, J=12.6Hz, ArCH ₂), 4.40 (2H, d, J=13.5Hz, ArCH ₂), 4.11 (6H, s, ArOCH ₃), 3.91 (6H, s, ArOCH ₃), 3.75 (6H, s, ArOCH ₃), 3.61 (2H, d, J=13.8Hz, ArCH ₂)	[α] _D ²² =89.55° (c0.22, CHCl ₃)	
57	Me	Me	H	3,4,5-F ₃ -C ₆ H ₂	H		δ7.92 (2H, d, J=8.4Hz, ArH), 7.20-7.57 (12H, m, ArH), 7.11 (2H, d, J=8.4Hz, ArH), 6.32 (2H, d, J=8.7Hz, ArH), 4.55 (2H, d, J=13.8Hz, ArCH ₂), 4.47 (4H, d, J=14.1Hz, ArCH ₂), 4.18 (2H, d, J=14.1Hz, ArCH ₂), 3.61 (2H, d, J=12.9Hz, ArCH ₂), 2.45 (6H, s, ArCH ₃), 2.05 (6H, s, ArCH ₃)		

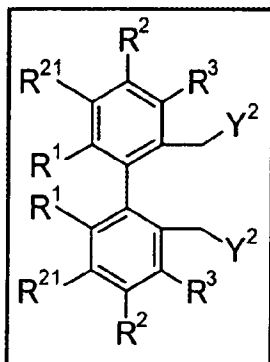
[0150]

Table 2

Optically active quaternary ammonium salt (1)											
											
Compound No.	R ¹	R ²	R ²¹	R ³	R ⁴	R ⁵	R ⁶	x	Physical property value (¹ HNMR, 300MHz, CDCl ₃)	Physical property (angle of rotation)	Note
32	Me	H	Me	3,4,5-F ₃ -C ₆ H ₂	H	H	OMe	Br	δ7.41 (4H, s, ArH), 7.00 (2H, d, J=8.7Hz, ArH), 6.85-6.91 (4H, m, ArH), 5.70 (2H, d, J=6.9Hz, ArH), 4.56 (2H, d, J=14.1Hz, ArCH ₂), 4.40 (2H, d, J=13.2Hz, ArCH ₂), 3.86 (2H, d, J=13.5Hz, ArCH ₂), 3.75 (6H, s, OCH ₃), 3.45 (2H, d, J=12.9Hz, ArCH ₂), 2.48 (6H, s, ArCH ₃), 2.04 (6H, s, ArCH ₃)		

[0151]

Table 3



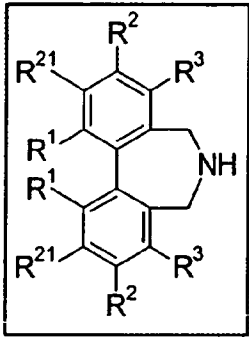
Compound No.	R ¹	R ²	R ²¹	R ³	Y ²	Physical property value (¹ HNMR, 300MHz, CDCl ₃)
22	Me	H	Me	3,4,5-F ₃ -C ₆ H ₂	Br	δ7.15 (2H, d, J=6.6Hz, ArH), 7.12 (2H, d, J=6.6Hz, ArH), 7.09 (2H, s, ArH), 4.03 (4H, d, J=2.4Hz, ArCH ₂), 2.37 (6H, s, ArCH ₃), 1.97 (6H, s, ArCH ₃)
44	OMe	OMe	OMe	3,4,5-F ₃ -C ₆ H ₂	Br	δ6.95-7.15 (4H, m, ArH), 3.90-4.00 (4H, m, ArCH ₂ O-), 3.95 (6H, s, ArOCH ₃), 3.87 (6H, s, ArOCH ₃), 3.73 (6H, s, ArOCH ₃)
47B	OMe	H	C ₆ H ₅	C ₆ H ₅	Br	87.30-7.68 (22H, m, ArH), 4.34 (4H, d, J=2.1Hz, ArCH ₂), 3.37 (6H, s, ArOCH ₃)
48B	OMe	H	4-CF ₃ -C ₆ H ₄	4-CF ₃ -C ₆ H ₄	Br	δ7.60-7.78 (16H, m, ArH), 7.34 (2H, s, ArH), 4.27 (4H, s, ArCH ₂), 3.38 (6H, s, ArOCH ₃)
49B	OMe	H	4-F-C ₆ H ₄	4-F-C ₆ H ₄	Br	δ7.60-7.78 (16H, m, ArH), 7.34 (2H, s, ArH), 4.27 (4H, s, ArCH ₂), 3.38 (6H, s, ArOCH ₃)
50B	OMe	H	3-CF ₃ -C ₆ H ₄	3-CF ₃ -C ₆ H ₄	Br	87.55-7.93 (16H, m, ArH), 7.35 (2H, s, ArH), 4.25 (4H, s, ArCH ₂), 3.37 (6H, s, ArOCH ₃)
51B	OMe	H	3,5-CF ₃ -C ₆ H ₃	3-CF ₃ -C ₆ H ₄	Br	δ7.90-8.15 (12H, m, ArH), 7.39 (2H, s, ArH), 4.17 (4H, s, ArCH ₂), 3.41 (6H, s, ArOCH ₃)
52B	OMe	OMe	H	3,5-CF ₃ -C ₆ H ₃	Br	87.81-7.92 (6H, m, ArH), 6.65 (2H, s, ArH), 3.81-3.92 (4H, m, ArCH ₂), 3.83 (6H, s, ArOCH ₃), 3.79 (6H, s, ArOCH ₃)
53B	OMe	H	OMe	3,5-CF ₃ -C ₆ H ₃	Br	88.02 (4H, s, ArH), 7.94 (2H, s, ArH), 6.87 (2H, s, ArH), 4.04 (4H, s, ArCH ₂), 3.95 (6H, s, ArOCH ₃), 3.86 (6H, s, ArOCH ₃)

(continued)

Compound No.	R ¹	R ²	R ²¹	R ³	Y ²	Physical property value (¹ HNMR, 300MHz, CDCl ₃)
54B	OMe	H	H	3,5-CF ₃ -C ₆ H ₃	Br	δ8.01 (4H, s, ArH), 7.91 (2H, s, ArH), 7.32 (2H, d, J=8.4Hz, ArH), 7.08 (2H, d, J=8.4Hz, ArH), 4.02 (4H, d, J=3.0Hz, ArCH ₂), 3.80 (6H, s, ArOCH ₃)
55B	OMe	H	H	3,4,5-F ₃ -C ₆ H ₂	Br	δ7.26 (2H, d, J=8.4Hz, ArH), 7.03 (2H, d, J=8.4Hz, ArH), 7.10-7.17 (4H, m, ArH), 4.06 (4H, s, ArCH ₂), 3.77 (6H, s, ArOCH ₃)
56B	OMe	OMe	OMe	3,5-CF ₃ -C ₆ H ₃	Br	δ6.95-7.15 (4H, m, ArH), 3.90-4.00 (4H, m, ArCH ₂ O-), 3.95 (6H, s, ArOMe), 3.87 (6H, s, ArOMe), 3.73 (6H, s, ArOMe)
57B	Me	Me	H	3,4,5-F ₃ -C ₆ H ₂	Br	δ7.15 (2H, d, J=6.6Hz, ArH), 7.12 (2H, d, J=6.6Hz, ArH), 7.09 (2H, s, ArH), 4.03 (4H, d, J=2.4Hz, ArCH ₂), 2.37 (6H, s, ArCH ₃), 1.97 (6H, s, ArCH ₃)

[0152]

Table 4

						
Compound No.	R ¹	R ²	R ²¹	R ³	Physical property value (¹ HNMR, 300MHz, CDCl ₃)	
23	Me	H	Me	3,4,5-F ₃ -C ₆ H ₂	87.31 (2H, s, ArH), 7.24 (2H, d, J=6.6Hz, ArH), 7.21 (2H, d, J=6.6Hz, ArH), 4.14 (2H, d, J=13.8Hz, ArCH ₂), 3.46 (2H, d, J=13.8Hz, ArCH ₂), 2.43 (6H, s, ArCH ₃), 2.09 (6H, s, ArCH ₃)	
47A	OMe	H	C ₆ H ₅	C ₆ H ₅	δ7.33-7.69 (22H, m, ArH), 3.95 (4H, d, J=12.6Hz, ArCH ₂), 3.41 (4H, d, J=12.6Hz, ArCH ₂), 3.29 (6H, s, ArOCH ₃)	
48A	OMe	H	H	3,5-CF ₃ -C ₆ H ₃	δ7.96 (4H, s, ArH), 7.85 (2H, s, ArH), 7.38 (2H, d, J=8.4Hz, ArH), 7.08 (2H, d, J=8.4Hz, ArH), 3.91 (6H, s, ArOCH ₃), 3.72 (2H, d, J=12.6Hz, ArCH ₂), 3.34 (2H, d, J=12.9Hz, ArCH ₂)	

(continued)

Compound No.	R ¹	R ²	R ²¹	R ³	Physical property value (¹ HNMR, 300MHz, CDCl ₃)
56A	OMe	OMe	OMe	3,5-CF ₃ -C ₆ H ₃	δ8.32 (2H, s, ArH), 7.76 (2H, s, ArH), 7.63 (2H, s, ArH), 3.98 (6H, s, ArOCH ₃), 3.87 (6H, s, ArOCH ₃), 3.67 (6H, s, ArOCH ₃), 3.45-3.76 (4H, m, ArCH ₂); m.p.=258-260° (decomp.)
57A	Me	H	Me	3,4,5-CF ₃ -C ₆ H ₂	δ7.00-7.22 (6H, m, ArH), 3.72 (2H, d, J=12.6Hz, ArCH ₂), 3.10 (2H, d, J=12.6Hz, ArCH ₂), 2.37 (6H, s, ArCH ₃), 2.06 (6H, s, ArCH ₃)

Reference Example

Asymmetric synthesis of α -amino acid using optically active quaternary ammonium salt compound (29)

[0153] 74 mg of tert-butyl(benzhydrylideneamino)acetate, 2.0 mg of an optically active quaternary ammonium salt compound (R, R)-(29), and 36 μ l of benzylbromide were added to 2 ml of a toluene solvent at 0°C. 0.5 ml of 50% KOH aqueous solution was added dropwise to the resulting solution while stirring. The reaction solution was stirred for 8 hours at 0°C and thereafter extracted by adding water and ether. The reaction product was purified by column chromatography (hexane: ether = 15: 1) to obtain targeted tert-butyl-2-(benzhydrylideneamino)-3-phenylpropionate (yield was 95%). Furthermore, optical purity was determined by HPLC analysis (hexane: isopropyl alcohol = 100: 1) using CHIRALCEL[®] OD manufactured by Daicel Chemical Industries, Ltd (asymmetric yield was 97% ee).

Reference Example 2

Asymmetric synthesis of α -amino acid using optically active quaternary ammonium salt compound (45)

[0154] When the same reaction as in the above Reference Example 1 was carried out using the catalyst represented by the formula (45), a corresponding alkylated substance was obtained with a yield of 96% and asymmetric yield of 94% ee.

Reference Example 3

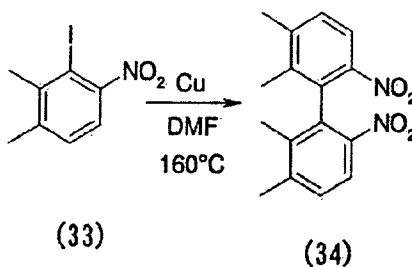
Asymmetric synthesis of α -amino acid using optically active quaternary ammonium salt compound (46)

[0155] When the same reaction as in the above Reference Example 1 was carried out using the catalyst represented by the formula (46), a corresponding alkylated substance was obtained with a yield of 100% and asymmetric yield of 98% ee.

Reference Example 4

Production of 2,3,2',3'-tetramethyl-6,6'-dinitrobiphenyl (34)

[0156]



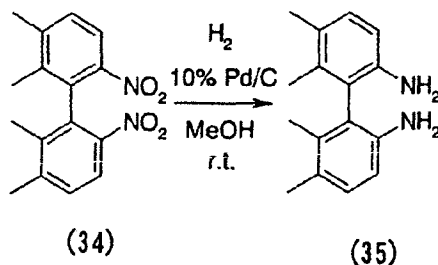
[0157] In 20 ml of a DMF solvent, 5.5 g (20 mmol) of 2-iodo-3,4-dimethyl-1-nitrobenzene and 10 g (155 mmol) of copper powder were heated at 150°C for 48 hours. After the completion of the reaction, copper powder was removed by filtration and thereafter, the resultant was extracted using ethyl acetate, dried/concentrated, and then purified by column chromatography (ethyl acetate: hexane = 1: 10) to obtain 2.9 g (0.96 mmol) of 2,3,2',3'-tetramethyl-6,6'-dinitro-

biphenyl (34) (yield was 96%).
¹H NMR (300MHz, CDCl₃), δ7.91 (2H, d, J=8.4Hz, ArCH), 7.34 (2H, d, J=8.4Hz, ArCH), 2.40 (6H, s, ArCH₃), 1.84 (6H, s, ArCH₃)

Reference Example 5

Production of 5,6,5',6'-tetramethylbiphenyl-2,2'-diamine (35)

[0158]



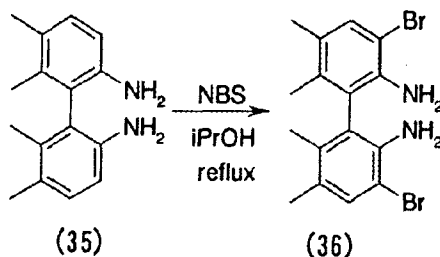
[0159] 3.0 g (10 mmol) of the compound (34) and 500 mg (5 mol%) of 10% Pd/C were added to 50 ml of a methanol solvent and were stirred for 12 hours under hydrogen atmosphere. After the completion of the reaction, solid matter was removed by filtration and thereafter, the resultant was purified by column chromatography (ethyl acetate: hexane = 1: 5) to obtain 2.4 g (10 mmol) of 5,6,5',6'-tetramethylbiphenyl-2,2'-diamine (35) (yield was 100%).

¹H NMR (300MHz, CDCl₃), δ6.97 (2H, d, J=8.1Hz, ArH), 6.58 (2H, d, J=8.4Hz, ArH), 3.25 (4H, br, NH₂), 2.21 (6H, s, ArCH₃), 1.86 (6H, s, ArCH₃)

Reference Example 6

Production of 3,3'-dibromo-5,6,5',6'-tetramethylbiphenyl-2,2'-diamine (36)

[0160]



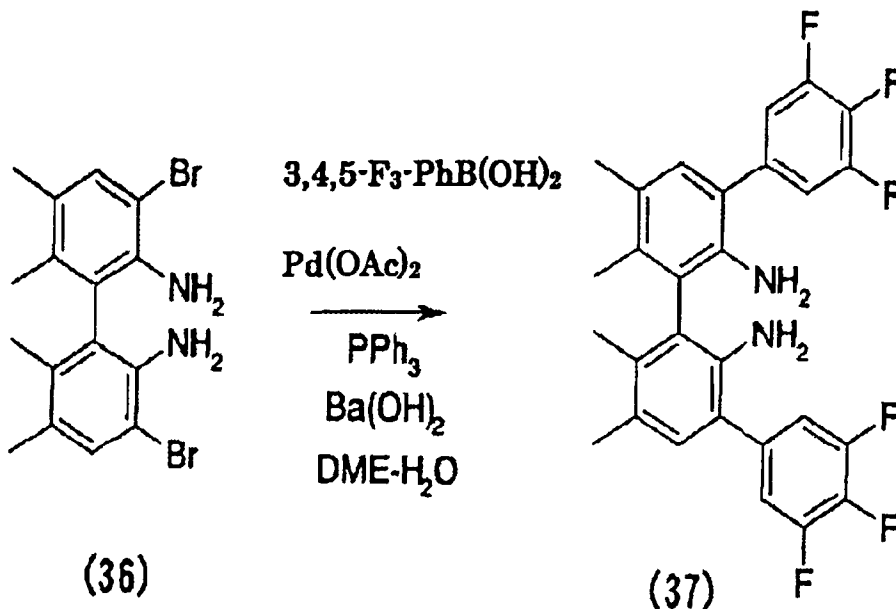
[0161] After dissolving 2.75 g (11.5 mmol) of the compound (35) in 20 ml of isopropyl alcohol, 4.45 g (25 mmol) of NBS was added thereto at 60°C. The reaction mixture was stirred for 1 hour under reflux and thereafter, poured into ice-cold water to stop the reaction. The obtained suspension was extracted with ethyl acetate and the resultant was dried/concentrated and thereafter purified by column chromatography (ethyl acetate: hexane = 1: 10) to obtain 2.98 g (7.48 mmol) of 3,3'-dibromo-5,6,5',6'-tetramethylbiphenyl-2,2'-diamine (36) (yield was 65%).

¹H NMR (300MHz, CDCl₃), δ7.27 (2H, s, ArH), 3.71 (4H, br, NH₂), 2.21 (6H, s, ArCH₃), 1.80 (6H, s, ArCH₃)

Reference Example 7

3,4,5,3''',4''',5'''-hexafluoro-4',5',4'',5''-tetramethyl-(1,1';3',3'';1'',1''')quaterphenyl-2',2''-diamine (37)

[0162]



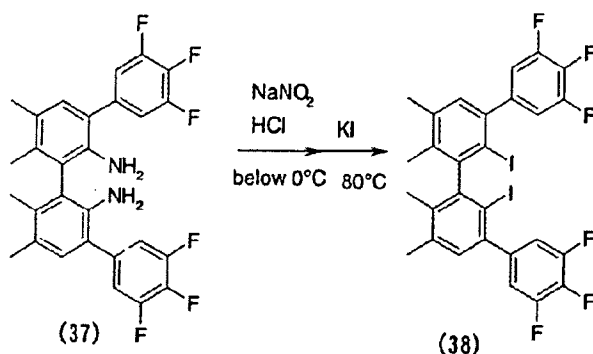
[0163] 1.5 g (3.77 mmol) of the compound (36), 1.5 g (9.0 mmol) of 3,4,5-trifluorophenylborate, 42 mg (5 mol%) of Pd(OAc)₂, 99 mg (10 mol%) of PPh₃, and 3.78 g (12.0 mmol) of Ba(OH)₂·8H₂O were added to 10 ml of a DME-H₂O (9:1 (v/v)) solvent and were stirred for 12 hours at 100°C under argon atmosphere. After the completion of the reaction, the obtained reaction mixture was poured into a saturated NH₄Cl solution and thereafter, the catalyst was removed by celite filtration. Furthermore, the resulting solution was extracted with ethyl acetate, dried/concentrated, and then purified by column chromatography (ethyl acetate: hexane = 1: 10) to obtain 1.63 g (3.21 mmol) of the compound (37) (yield was 85%).

¹H NMR (300MHz, CDCl₃), δ7.15 (2H, d, J=6.6Hz, ArH), 7.12 (2H, d, J=6.6Hz, ArH), 6.92 (2H, s, ArH), 3.46 (4H, br, NH₂), 2.26 (6H, s, ArCH₃), 1.92 (6H, s, ArCH₃)

Reference Example 8

Production of 2',2''-diiodo-3,4,5,3''',4''',5'''-hexafluoro-4',5',4'',5''-tetramethyl-(1,1';3',3'';1'',1''')quaterphenyl (38)

[0164]



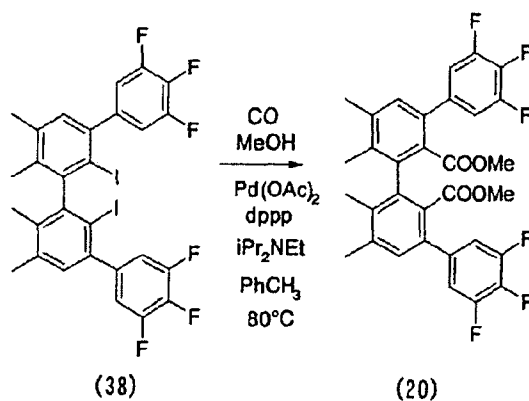
[0165] 760 mg (1.52 mmol) of the compound (37) was dissolved in 20 ml of 6M HCl and the resulting solution was cooled down to 0°C. 315 mg (4.56 mmol) of NaNO₂ aqueous solution was slowly added dropwise to this solution in 5 minutes. Furthermore, 1.51 g (9.12 mmol) of KI aqueous solution was added dropwise thereto at the same temperature and the reaction temperature was increased to 80°C after the addition. After stirring the reaction mixture for another 2 hours at the same temperature, it was cooled using ice-cold water and the reaction was stopped by adding sodium sulfite thereto. The obtained mixture was extracted with diethylether and the resultant was dried/concentrated and thereafter purified by column chromatography (ethyl acetate: hexane = 1: 10) to obtain 1.03 g (1.43 mmol) of the compound (38) (yield was 94%).

¹H NMR (300MHz, CDCl₃), 87.09 (2H, s, ArH), 6.99 (2H, d, J=7.2Hz, ArH), 6.97 (2H, d, J=6.6Hz, ArH), 2.33 (6H, s, ArCH₃), 1.99 (6H, s, ArCH₃)

Reference Example 9

Production of 3,4,5,3'',4'',5'''-hexafluoro-4',5',4'',5'''-tetramethyl-(1,1';3',3'';1'',1''')quaterphenyl-2',2''-dimethyl dicarbonate (20)

[0166]

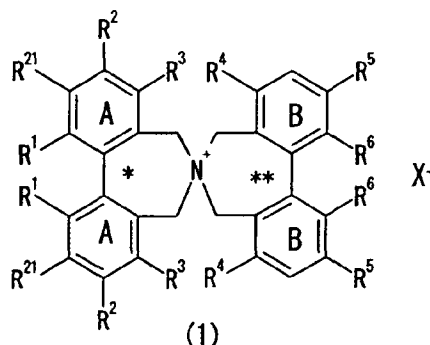


[0167] 361 mg (0.5 mmol) of the compound (38), 5.6 mg (5 mol%) of Pd(OAc)₂, 10.3 mg (5 mol%) of 1,3-bis(diphenylphosphino)propane, 0.52 ml (3 mmol) of N-ethyl-diisopropylamine, and 3ml of MeOH were added to 3 ml of a toluene solvent and were stirred for 48 hours at 80°C under 10 atm of carbon monoxide. After the completion of the reaction, the catalyst was removed by filtration and thereafter, the resultant was purified by column chromatography (ethyl acetate: hexane = 1: 20) to obtain 198 mg (0.34 mmol) of the compound (20) (yield was 68%).

¹H NMR (300MHz, CDCl₃), 87.14 (2H, s, ArH), 6.99 (2H, d, J=6.6Hz, ArH), 6.94 (2H, d, J=6.3Hz, ArH), 3.27 (6H, s, ArH), 2.40 (6H, s, ArCH₃), 1.97 (6H, s, ArCH₃)

Claims

1. An optically active quaternary ammonium salt compound represented by formula (1),

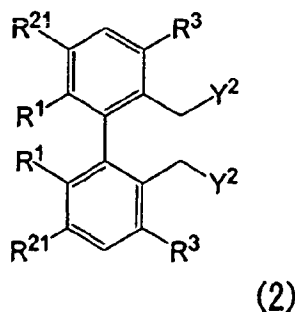


wherein R¹ represents a halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;
 R² and R²¹ each independently represents hydrogen, halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;
 one of combinations of R¹ and R²¹, and R² and R²¹, may bond to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylenemonooxy which is optionally substituted, or a C₁₋₆ alkylenedioxy which is optionally substituted;
 R³ and R⁴ each independently represents hydrogen, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, with a proviso that R³ and R⁴ are not hydrogen at the same time;
 R⁵ represents hydrogen, halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, or a C₂₋₈ alkynyl which is optionally substituted;
 R⁶ represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, or a C₂₋₈ alkynyl which is optionally substituted, and R⁵ and R⁶ may bond to form an aromatic ring which is optionally substituted;
 ring A and ring B do not have a same substituent at the same time;
 symbols * and ** represent an optical activity having an axial chirality; and
 X⁻ represents an anion.

2. The compound according to Claim 1,
 wherein R² is hydrogen and R²¹ is halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted.
3. The compound according to Claim 1,
 wherein R¹, R², and R²¹ each independently represents a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic.
4. The compound according to Claim 1,
 wherein R¹ is a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, and R² and R²¹ bond to form a C₁₋₆ alkylenedioxy which is optionally substituted.
5. The compound according to Claim 1,

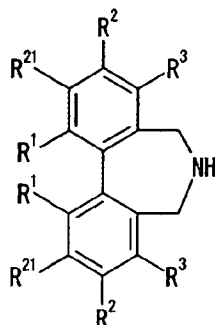
wherein R¹ and R²¹ each independently represents a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, and R² is hydrogen.

6. The compound according to any one of Claims 1 to 4,
 wherein R³ represents a C₆₋₁₄ aryl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl), a C₃₋₈ heteroaryl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl), or a C₇₋₁₆ aralkyl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl); and
 R⁴ is hydrogen.
7. The compound according to any one of Claims 1 to 4,
 wherein R³ represents hydrogen; and
 R⁴ is a C₆₋₁₄ aryl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl), a C₃₋₈ heteroaryl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl), or a C₇₋₁₆ aralkyl (which is optionally substituted by halogen, a C₁₋₈ alkyl which is optionally substituted by halogen and which is linear, branched, or cyclic, or a C₆₋₁₄ aryl).
8. The compound according to any one of Claims 1 to 7,
 wherein X⁻ is an anion of halogen, OH⁻, BF₄⁻, PF₆⁻, HSO₄⁻, an anion of C₁₋₆ dialkylsulfate which is optionally substituted and which is linear, branched, or cyclic, an anion of C₁₋₆ alkylsulfonate which is optionally substituted and which is linear, branched, or cyclic, an anion of C₆₋₁₄ arylsulfonate which is optionally substituted, or an anion of C₇₋₁₆ aralkylsulfonate which is optionally substituted.
9. An optically active bisbenzyl compound or a racemic bisbenzyl compound represented by formula (2) and which has an axial chirality,



wherein R¹ represents a halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;
 R²¹ each independently represents hydrogen, halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;
 R¹ and R²¹ may bond to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylenemonooxy which is optionally substituted, or a C₁₋₆ alkylenedioxy which is optionally substituted;
 R³ represents hydrogen, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted; and
 Y² represents a leaving group.

10. An optically active azepine derivative or a racemic azepine derivative represented by formula (3),



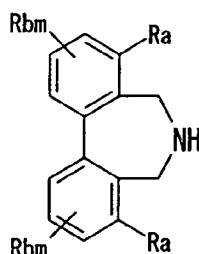
(3)

wherein R¹ represents a halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;

R² and R²¹ each independently represents hydrogen, halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;

one of combinations of R¹ and R²¹, and R² and R²¹, may bond to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylidenedioxy which is optionally substituted, or a C₁₋₆ alkylidenedioxy which is optionally substituted; and R³ represents hydrogen, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted.

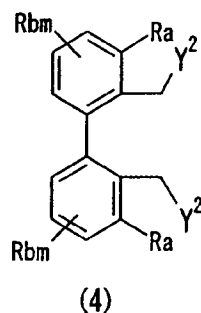
11. A production method of an azepine derivative represented by formula (5)



(5)

comprising:

reacting a biphenyl derivative represented by formula (4)



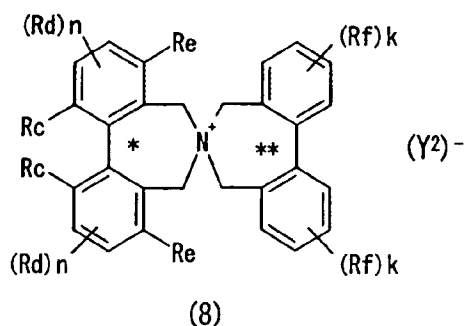
with ammonia,

wherein Ra represents a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted;

Rb represents halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted, and Rb may bond with each other to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylene monooxy which is optionally substituted, a C₁₋₆ alkylene dioxy which is optionally substituted, or an aromatic ring which is optionally substituted; and

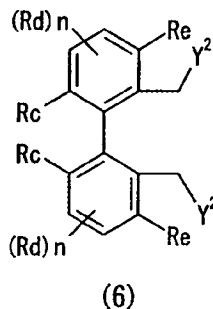
m is 0 or represents an integer of 1 to 3 and Rb may be different substituents to each other when m is 2 or more.

12. A production method of an optically active quaternary ammonium salt compound represented by formula (8)

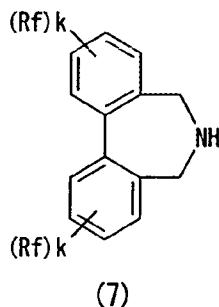


comprising:

reacting an optically active bisbenzyl derivative represented by formula (6)



with a racemic azepine derivative represented by formula (7)



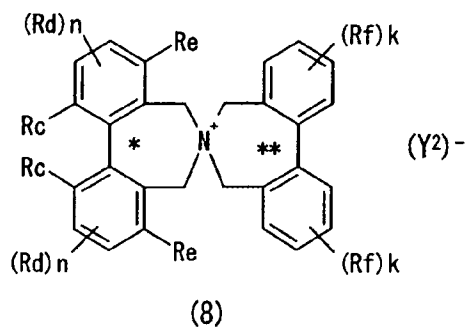
wherein Rc represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;

Rd and Re each independently represents halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, and Rd may bond with each other to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylidenedioxy which is optionally substituted, or a C₁₋₆ alkylidenedioxy which is optionally substituted, and n is 0 or represents an integer of 1 to 2 and Rd may be different substituents to each other when n is 2;

Y² represents a leaving group;

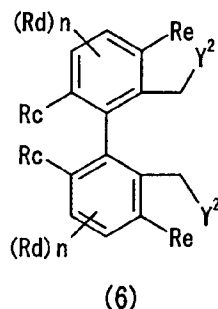
Rf represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, and k is 0 or represents an integer of 1 to 4 and Rf may be different substituents to each other when k is 2 or more and Rf may bond with each other to form an aromatic ring which is optionally substituted; and symbols * and ** represent an optical activity having an axial chirality.

13. A production method of an optically active quaternary ammonium salt compound represented by formula (8)

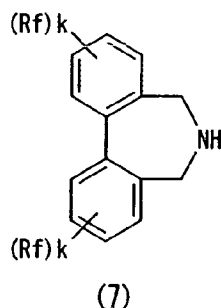


comprising:

reacting a racemic bisbenzyl derivative represented by formula (6)



with an optically active azepine derivative represented by formula (7)

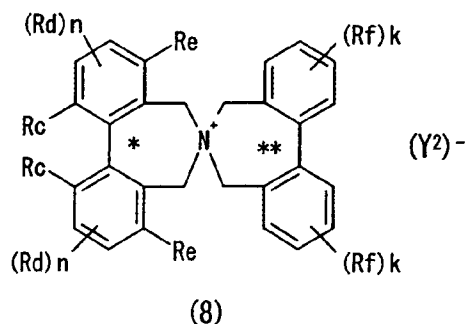


wherein Rc represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;

Rd and Re each independently represents halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, and Rd may bond with each other to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylenemonooxy which is optionally substituted, or a C₁₋₆ alkylenedioxy which is optionally substituted, and n is 0 or represents an integer of 1 to 2 and Rd may be different substituents to each other when n is 2, and Y² represents a leaving group;

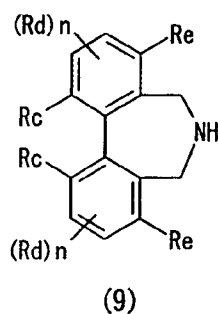
Rf represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, and k is 0 or represents an integer of 1 to 4 and Rf may be different substituents to each other when k is 2 or more and Rf may bond with each other to form an aromatic ring which is optionally substituted; and symbols * and ** represent an optical activity having an axial chirality..

14. A production method of an optically active quaternary ammonium salt compound represented by formula (8)

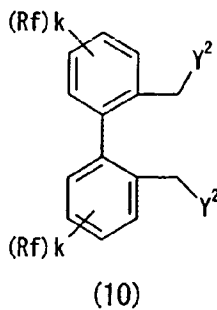


comprising:

reacting an optically active azepine derivative represented by formula (9)



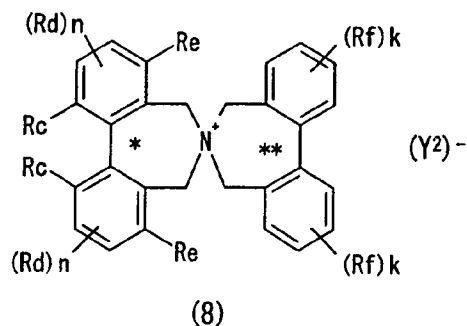
with a racemic bisbenzyl derivative represented by formula (10)



wherein Rc represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;
 Rd and Re each independently represents halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, and Rd may bond with each other to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylidenedioxy which is optionally substituted, or a C₁₋₆ alkylidenedioxy which is optionally substituted;
 n is 0 or represents an integer of 1 to 2 and Rd may be different substituents to each other when n is 2;
 Rf represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is

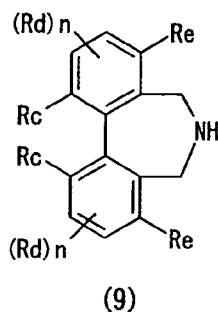
optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted; k is 0 or represents an integer of 1 to 4 and R_f may be different substituents to each other when k is 2 or more; Y² represents a leaving group; and symbols * and ** represent an optical activity having an axial chirality.

15. A production method of an optically active quaternary ammonium salt compound represented by formula (8)

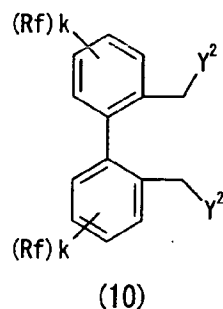


comprising:

reacting a racemic azepine derivative represented by formula (9)



with an optically active bisbenzyl derivative represented by formula (10)



wherein R_c represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, or a C₇₋₁₆ aralkyl which is optionally substituted;

Rd and Re each independently represents halogen, nitro, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted, and Rd may bond with each other to form a C₁₋₆ alkylene which is optionally substituted, a C₁₋₆ alkylenemonooxy which is optionally substituted, or a C₁₋₆ alkylenedioxy which is optionally substituted;

n is 0 or represents an integer of 1 to 2 and Rd may be different substituents to each other when n is 2;

Rf represents halogen, a C₁₋₈ alkyl which is optionally substituted and which is linear, branched, or cyclic, a C₁₋₈ alkoxy which is optionally substituted and which is linear, branched, or cyclic, a C₂₋₈ alkenyl which is optionally substituted, a C₂₋₈ alkynyl which is optionally substituted, a C₆₋₁₄ aryl which is optionally substituted, a C₃₋₈ heteroaryl which is optionally substituted, or a C₇₋₁₆ aralkyl which is optionally substituted;

k is 0 or represents an integer of 1 to 4 and Rf may be different substituents to each other when k is 2 or more;

Y² represents a leaving group; and

symbols * and ** represent an optical activity having an axial chirality.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2006/304091

A. CLASSIFICATION OF SUBJECT MATTER

C07D487/10(2006.01), C07D223/18(2006.01), C07C25/18(2006.01), C07C43/225(2006.01), C07B53/00(2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07B53/00, C07C25/18, C07C43/225, C07D223/18, C07D487/10

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Jitsuyo Shinan Koho	1922-1996	Jitsuyo Shinan Toroku Koho	1996-2006
Kokai Jitsuyo Shinan Koho	1971-2006	Toroku Jitsuyo Shinan Koho	1994-2006

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS (STN), REGISTRY (STN), MEDLINE (STN), EMBASE (STN), BIOSIS (STN), WPIDS (STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X P,A	JP 2005-225809 A (Nippon Soda Co., Ltd.), 25 August, 2005 (25.08.05), Par. No. [0082] (Family: none)	9 1-8, 12-15
P,X	JP 2005-225810 A (Nippon Soda Co., Ltd.), 25 August, 2005 (25.08.05), Par. Nos. [0048] to [0050]; the compound represented by the formula (4) (Family: none)	9
P,A	OOI, T. et al., Importance of Chiral Phase- Transfer Catalysts with Dual Functions in Obtaining High Enantioselectivity in the Michael Reaction of Malonates and Chalcone Derivatives, Organic Letters, 2005, Vol.7, No.15, pages 3195 to 3197	1-8, 12-15

☒ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search

25 May, 2006 (25.05.06)

Date of mailing of the international search report

06 June, 2006 (06.06.06)

Name and mailing address of the ISA/

Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2006/304091

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	OOI, T. et al., Design of New Chiral Phase-Transfer Catalysts with Dual Functions for Highly Enantioselective Epoxidation of α , β -Unsaturated Ketones, J.Am.Chem.Soc., 2004, Vol.126, pages 6844 to 6845	9,10 1-8,12-15
A	OOI, T. et al., Evaluation of the Relationship between the Catalyst Structure and Regio- as well as Stereoselectivity in the Chiral Ammonium Bifluoride-Catalyzed Asymmetric Addition of Silyl Nitronates to α , β -Unsaturated Aldehydes, Chemistry Letters, 2004, Vol.33, No.7, page 824 to 825	1-8,12-15
X	JP 2002-326992 A (Nagase & Co., Ltd.), 15 November, 2002 (15.11.02), Compounds (I), (III) (Family: none)	1-8,10,12-15
X	OOI, T. et al., Conformationally Flexible, Chiral Quaternary Ammonium Bromides for Asymmetric Phase-Transfer Catalysis, Angew.Chem.Int.Ed., 2002, Vol.41, No.9, pages 1551 to 1554	1-8,12-15
P,A	WO 2005/007622 A2 (Tosoh Corp.), 27 January, 2005 (27.01.05), The formula (16) in Par. No. [0017]; the formula (17), in Par. No. [0010] & JP 2005-41791 A & JP 2005-41792 A	1-8,12-15
X	JP 2004-238362 A (Tosoh Corp.), 26 August, 2004 (26.08.04), Claims 10, 15; Par. Nos. [0006] to [0009], [0020] (14), Par. Nos. [0131] to [0132] (Family: none)	1-15
X	COLLETTI, S. L. et al., Asymmetric Synthesis and Metalation of a Binaphthylcyclopentadiene, a C ₂ -Symmetric Chiral Cyclopentadiene, Organometallics, 1991, Vol.10, pages 3438 to 3448	9
P,X	WO 2005/077908 A1 (Takasago International Corp.), 25 August, 2005 (25.08.05), Par. Nos. [0048], [0049] to [0052]; examples (Family: none)	9
P,X	WO 2005/073196 A1 (Nagase & Co., Ltd.), 11 August, 2005 (11.08.05), Claim 9; formula (II); compound (Family: none)	9

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2006/304091

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	JP 2005-263664 A (Nagase & Co., Ltd.), 29 September, 2005 (29.09.05), Claim 2; examples; particularly, compounds (8), (9) (Family: none)	9,10
P,X	JP 2005-15402 A (Nagase & Co., Ltd.), 20 January, 2005 (20.01.05), Compounds I, III (Family: none)	9,10
X	WO 2004/076459 A1 (Nagase & Co., Ltd.), 10 September, 2004 (10.09.04), Claim 7; referential examples; particularly, compounds (8), (9) (Family: none)	9,10
X	JP 2004-352708 A (Nagase & Co., Ltd.), 16 December, 2004 (16.12.04), Par. Nos. [0104] to [0110]; compound (V'); referential examples; particularly, compounds (8), (9) (Family: none)	9,10
X	JP 2004-131447 A (Nagase & Co., Ltd.), 30 April, 2004 (30.04.04), Claims 3, 4; Par. Nos. [0115] to [0120]; compounds 1, 2 (Family: none)	9,10
X	JP 2003-327566 A (Nagase & Co., Ltd.), 19 November, 2003 (19.11.03), Compounds (18), (19) (Family: none)	9,10
X	JP 2003-81976 A (Nagase & Co., Ltd.), 19 March, 2003 (19.03.03), Claims 10, 20 (Family: none)	9,10
X	JP 2002-173492 A (Nagase & Co., Ltd.), 21 June, 2002 (21.06.02), Claims 15, 18 (Family: none)	9,10
X	JP 2001-48866 A (Nagase & Co., Ltd.), 20 February, 2001 (20.02.01), Claims 5, 7 & WO 2001/081349 A1 & EP 1277755 A1 & US 6340753 B1	9,10

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2006/304091

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP 8-40954 A (Hoechst AG.), 13 February, 1996 (13.02.96), Full text & EP 675095 A1 & US 5502261 A	9
X	IKUNAKA, M. et al., A Scalable Synthesis of (R)-3, 5-Dihydro-4H-dinaphth [2,1-c:1'2'- elazepine, Organic Process Research & Development, 2003, Vol.7, pages 644 to 648	9,10
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A	WO 1993/020695 A1 (SPHINX PHARACEUTICALS CORP.), 28 October, 1993 (28.10.93), Example 12 (Family: none)	10
X	JP 11-510802 A (The University of Sheffield), 21 September, 1999 (21.09.99), Compound (IV); page 11, step 2 & WO 1997/006147 A1 & EP 843664 A1 & US 6063920 A	9,10
A	JP 2004-359578 A (Nippon Soda Co., Ltd.), 24 December, 2004 (24.12.04), Full text (Family: none)	9

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REFERENCES CITED IN THE DESCRIPTION

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- *J. Chem. Soc.*, 1950, vol. 711 [0103]
- *J. Am. Chem. Soc.*, 1999, vol. 121, 6519 [0106]